

Overcoming Opioid Addictions with Traditional Chinese Medicine (TCM)

A Seven CEU/PDA Hour Course

Course Outline:

I. Course Objectives

II. Overview of Opioid Addictions in the USA

III. TCM Herbal and Nutritional Protocols for Opioid Addictions with Associated Peer-Reviewed Research

IV. Acupuncture Protocols for Treatment of Opioid and Other Addictions with Associated Peer-Reviewed Research

V. Other Strategies to Support Continued Sobriety

VI. Exam

I. Objectives of this course:

1. Students will gain an overview of the problem of opioid addictions.
2. Students will develop understanding of acupuncture, TCM herbal, and nutritional treatment strategies to deal with opioid withdrawal symptoms and to support continued sobriety.
3. Students will learn about peer-reviewed research which documents the efficacy of acupuncture and TCM herbal protocols for treating symptoms of opioids withdrawal.
4. Students will be introduced to other strategies to support continued sobriety.

II. Overview of Opioid Addictions in the USA

We in the USA are faced with a horrendous epidemic of opioid addictions. In 2016 over 30,000 Americans died from this disease. The pity of this ongoing tragedy is that Traditional Chinese Medicine (TCM) holds so many safe, inexpensive, and effective solutions to alleviate this crisis and avoid unneeded human suffering. Unfortunately these solutions are largely being ignored. Ironically, those who have created the problem are also primarily who stand in the way of the solutions.

Certainly the pharmaceutical industry bears much of the blame, pumping out these poisons by the tractor trailer load into cities and towns across the nation while drowning state and federal politicians in lobbying money to keep this drug-pushing racket legal. At the same time it cajoles the public to seek out drug treatments for pain with innumerable ads in print, on TV, and on the Internet. Even worse, the pharmaceutical industry has had an unseemly and disproportionate impact on the framing of curricula in America's medical schools. Virtually the only treatment tools doctors have upon graduation are drugs and surgery, both of which contribute to the over-prescription and overuse of opioids.

Without question the medical profession must assume a huge responsibility for over-prescribing opioids beyond any reasonable measure related to human health. Moreover, the AMA and its doctors deserve unmitigated calumny for NOT referring patients to acupuncturists, those very health care providers who are specialists in the treatment of pain without drugs. Since 1972 the AMA has resisted efforts by the acupuncture profession to gain a foothold in America's health care delivery system, a conspiracy well documented by Yale Professor Paul Root Wolpe in his publication, **The Maintenance of Professional Authority: Acupuncture and the American Physician**.

https://www.jstor.org/stable/800772?seq=1#page_scan_tab_contents

Abstract

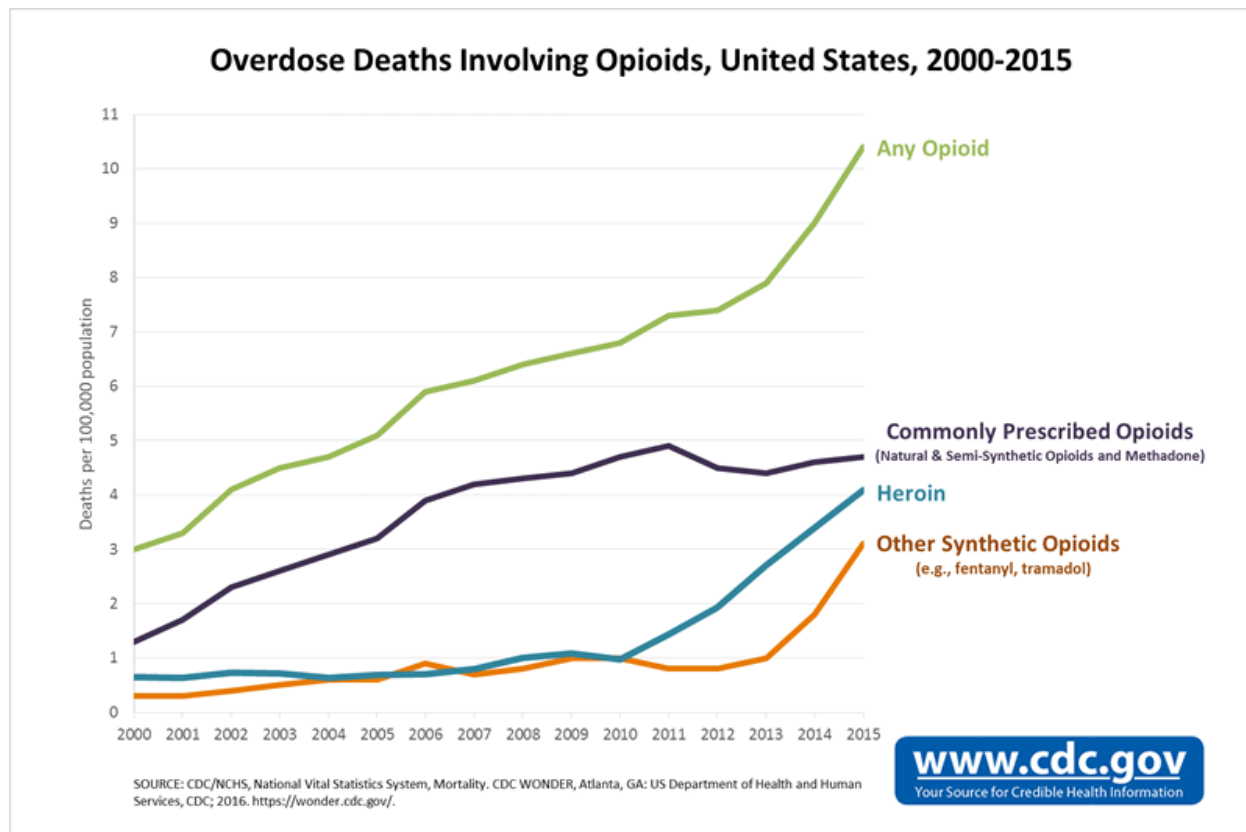
"This paper examines the response of the medical profession to a situation in which its cultural authority was potentially challenged: the sudden, large-scale importation of acupuncture into the United States in the early 1970s. I describe how the medical profession coped with a therapeutic modality that could not be explained by the biomedical model. Various tactics were used to limit the practice of acupuncture to physicians, thereby mitigating the threat of the growing popularity of lay practitioners. Once it was securely under the control of the medical profession, the practice of acupuncture was severely restricted, and an effective but enigmatic modality was removed from the medical regimen."

The US Federal Government shares in the blame as well for not regulating opioid properly and for discriminating against licensed acupuncturists in many tangible ways – such as

- preventing licensed acupuncturists from being included as providers under Medicare and Medicaid,

- not including licensed acupuncturists in federal tuition forgiveness programs
- severely limiting the role of licensed acupuncturists in the Veterans Administration health care system
- classifying acupuncture needles by the FDA as experimental devices and restricting their use only to hospital research settings

The US Centers for Disease Control (CDC) does attempt to address this crisis but in a most inadequate way. It publishes data documenting the extent of the epidemic.



The CDC even offers the following online courses:

1. **[Addressing the Opioid Epidemic: Recommendations from CDC](#)**

This module presents an overview of the CDC Guideline for Prescribing Opioids for Chronic Pain: It explains the rationale for the Guideline's creation, highlights key recommendations, and describes the benefits of implementing the Guideline.

2. **[Communicating With Patients](#)**

Providers will learn communication strategies they can use when treating chronic pain, including motivational interviewing.

3. **[Treating Chronic Pain Without Opioids](#)**

This module presents providers with an alternate vision for chronic pain treatment, giving them the tools they need to use non-opioid options.

4. **Deciding Whether to Prescribe**

In this section of the training, providers learn mechanisms for deciding whether or not to prescribe opioids, and next steps or alternate treatments for both courses of action.

5. **Dosing and Titration of Opioids: How Much, How Long, and How and When to Stop?**

When providers choose to prescribe opioids, they need to know how to properly dose and titrate opioids to reduce risk of opioid abuse. This module explains methods of dosing and titration.

6. **Reducing the Risks of Opioids**

Providers will learn best risk mitigation strategies and when to employ them after prescribing an opioid.

7. **Assessing and Addressing Opioid Use Disorder**

This module describes methods available to a provider for assessing and addressing an opioid use disorder when it is suspected.

8. **Implementing the CDC Guideline**

This module provides strategies and tools for implementing the CDC Guideline for Prescribing Opioids for Chronic Pain in a provider's own practice, while outlining steps to overcome common barriers to implementation.

However, more draconian measures are obviously needed. Why they have not been undertaken is a testament to the perverse and parasitic power of America's pharmaceutical industry to lobby Congress. From 1997 to 2017 Big Pharma spent \$3,591,294,472 on its federal lobbying efforts, tops among all industries. Meanwhile, Licensed Acupuncturists, who are excellent at treating symptoms of acute and chronic pain, spent less than \$50,000 during this time period on federal lobbying. I know, having personally chaired the legislative committee of the American Association of Acupuncture and Oriental Medicine during its fruitless drive to get acupuncturists included as Medicare providers. The use of acupuncture and TCM herbal protocols should be widely supported by government to avoid the need to prescribe opioids. Instead these protocols are basically ignored or stymied.

Acupuncture and TCM herbal therapies, though largely ignored, are also very helpful to alleviate these early and late symptoms of opioid withdrawal:

Early Withdrawal Symptoms start within 6 to 30 hours:

- Agitation
- Anxiety
- Cravings
- Depression
- Excessive Yawning
- Fever
- Hypertension
- Muscle Aches and Cramping
- Nausea
- Nose running

- Sweats
- Tachycardia

Late Withdrawal Symptoms can be most intense around 72 hours and can last a week or more:

- Cramps of the Digestive System
- Depression
- Diarrhea
- Goosebumps
- Nausea
- Opioid Cravings

The Spanish essayist, novelist, philosopher, and poet Jorge Agustín Nicolás Ruiz de Santayana y Borrás once wrote:

"Those who cannot remember the past are condemned to repeat it."

That saying is often misquoted as

"Those who do not know history's mistakes are doomed to repeat them."

In either case those thoughts offer wise counsel to us today. Ironically and sadly, America has much to learn from Chinese medicine, because the West has already run this experiment before of addicting millions of people to opioids and of standing by to watch what happened. For two centuries the Chinese were victims of such malevolence, and by necessity they had to devise ways to counter opioid addictions using Traditional Chinese Medicine (TCM)...ways which we shall explore - but first, a little history.

Few Westerners know about the suffering which the Chinese people experienced at the hands of the British, who in the 19th century repeatedly waged wars against China - principally to maintain an unrestricted ability to foster addiction to opium and to supply an ever growing number of Chinese addicts with opium. Again, we face a similar crisis in the USA given the collusion of the US federal and state governments and their regulatory agencies with the medical profession and the pharmaceutical industry, a connection too few recognize.

"This war with China . . . really seems to me so wicked as to be a national sin of the greatest possible magnitude, and it distresses me very deeply. Cannot anything be done by petition or otherwise to awaken men's minds to the dreadful guilt we are incurring? I really do not remember, in any history, of a war undertaken with such combined injustice and baseness. Ordinary wars of conquest are to me far less wicked, than to go to war in order to maintain smuggling, and that smuggling consisting in the introduction of a demoralizing drug, which the government of China wishes to keep out, and which we, for the lucre of gain, want to introduce by force; and in this quarrel are going to burn and slay in the pride of our supposed superiority."

- [Thomas Arnold](#) to W. W. Hull, March 18, 1840

The following quotes and charts derive from this source:

The Consumption of Opium in China

Philip V. Allingham, Contributing Editor, Victorian Web; Lakehead University, Thunder Bay, Ontario

<http://www.victorianweb.org/history/empire/opiumwars/opiumwars2.html>

By the 1840's "as the habit of [smoking opium spread](#) from the idle rich to ninety per cent of all Chinese males under the age of forty in the country's coastal regions, business activity was much reduced, the civil service ground to a halt, and the standard of living fell."

The financial rewards to British and then also to American merchants were enormous. By 1840 the Chinese were importing over 5,000 tons of opium annually from the British and Americans.

"...whereas prior to 1810 Western nations had been spending 350 million Mexican silver dollars on porcelain, cotton, silks, brocades, and various grades of tea, by 1837 [over 5,000 tons of] opium represented 57 per cent of Chinese imports, and for fiscal 1835-36 alone China exported 4.5 million silver dollars."

Year	Chests	Value in Dollars
1816	3,210	3,657,000
1820	4,770	8,400,800
1825	9,621	7,608,205
1830	18,760	12,900,031
1832	23,670	15,338,160
1836	27,111	17,904,248

Company, we can see silver, approximately annually by the mid-result of British trading and cultivating lands it

Year	Chests	Value in Dollars
1827-28	9,535	10,425,075
1828-29	13,132	12,533,105
1829-30	14,000	12,057,157
1830-31	18,760	12,904,263
1831-32	14,225	11,501,584
1832-33	23,603.5	15,252,429
1833-34	21,250	14,006,605
1834-35	20,089	11,758,779
1835-36	26,018	17,106,903

Chests of Opium Exported to China by the British and their Value in Dollars

1816-1836

[Source: Thelwall, pp. 33-34]

1827-1835

[Source: Edmonds, p. 10]

"Since most of the opium came from India, either from the Princely States or the plantations of the British East India that the net outflow of fifteen million dollars 1830s, was the direct policy. The cost of clearing had recently acquired in

the Bombay region and in Burma required that the British East India Company make vast profits, and it did so by undermining the health and government of 300,000,000 Chinese. In 1834-35 alone, the B. E. I. Co. exported 10,107 chests from Calcutta to China, chiefly the port of Canton. However, the B. E. I. Company's flooding the market in 1831-32 resulted in the price of a chest of opium dropping from \$2,075 (average for 1821-22) to just \$955. although thanks to the cancellation of the B. E. I. Company's monopoly in 1834 profits in the trade dropped from 9,413,091 Rupees to 6,827,628 (despite a sharp increase in shipments to China), by 1848-49 the profits rose to 24,103,775 rupees, presumably because of an ever-increasing number of addicts in China. — Kuo, p. 32”

As a result of the opium wars and its effects, China itself was torn asunder, lost its sovereignty, and was partitioned by Western powers which dictated its terms of trade. Addiction to opiates was widespread in China until Mao's revolution of 1949, when there were 70 million junkies addicted to morphine, opium, and heroin in a population of 700 million!

This was a severe national health crisis in China, one which the new revolutionary government quickly overcame. How so?

Clark Kissinger says this on his website, <http://revcom.us/a/china/opium.htm> :

“In China, the Maoist revolution ended drug addiction QUICKLY. Mao's revolutionary armies defeated the oppressors' armies in 1949. THREE YEARS LATER, in 1952, there were no more addicts, no more pushers, no more opium poppies grown, and no more drugs smuggled in. In only three short years China went from 70 million drug addicts to none...”

“In China, the revolution created a People's Liberation Army and then a new People's Government. This government and the revolutionary masses were led by the Maoist vanguard party, the Communist Party of China. When the revolution won in 1949, the power in society SERVED THE PEOPLE for the first time, not the oppressors. There were big problems of all kinds, left over from the old society. But now it was possible for the people to be organized in their own interests to solve those problems.

“From the first months of the NEW POWER, the revolution used the Maoist method of MASS LINE to take on drug addiction. This campaign did not rely on social workers talking down to the people or on punishments. The revolutionary communists relied on THE MASSES OF PEOPLE -- throughout cities and countryside -- to organize themselves to end drug manufacturing, sale and use.

“The Maoist revolutionaries called on the addicts themselves to step forward, kick their habit and join the struggle for a new society. The Maoist revolutionaries organized the people in the communities to struggle with their addicted brothers and sisters: to persuade them and educate them. Ex-addicts and their families joined big marches and rallies. Drugs were burned at neighborhood celebrations. Kids were organized in their schools. The NEW POWER meant that the newspapers and radio were mobilized to support the revolutionary campaign.

“It was hard to kick the habit, and many addicts resisted at first. But the masses knew if an addict was still copping drugs. Children argued with parents. Wives argued with husbands. Everyone asked the addicts to get with the new society.

“At the same time, the revolutionaries organized the people to bust up the business networks that sold drug poison to the people. This meant that supplies were disappearing -- it was getting harder and harder for addicts to stay high.

“In short, the struggle against drug addiction became a large-scale mass movement -- the kind of mass movement only a true revolutionary government of the people can create.”

What Kissinger neglects to mention were the practical steps people undertook using TCM to alleviate withdrawal symptoms and to restore health. In the USA we need to adopt the will China exhibited - if not the techniques - to prevent widespread, improper distribution of pharmaceutical and illegal opioids. We also need the US federal and state governments to support use of the herbal, nutritional, and acupuncture protocols which follow.

III. TCM Herbal Treatments and Nutritional Protocols for Opioid Addictions

A. Meeting Lauren Laks, L.Ac., MSTCM

I was asked to prepare this course by Steven Paine, President of the National Guild for Acupuncture and Oriental Medicine, OPEIU #62, AFL-CIO who is as alarmed by the opioid epidemic as I am. In the process of researching herbal approaches, I came upon an absolute

angel of a practitioner, Lauren Laks, L.Ac., MSTCM. During our correspondence she alerted me to a great deal of research on the best herbal approaches to resolving opioid addictions, which I am please to share with you here. As a matter of full disclosure, I have no financial relationship with Lauren and derive no reward nor recompense whatsoever from the sale of any products she suggests, other than the serenity which comes by knowing others will be helped. What follows is an introduction to our discussion.

Dear Lauren, I am writing a course for NGAOM, NCCAOM, Florida, and for California acupuncture CEU credits on withdrawing from opioid addiction. I was really fascinated by your website:

<https://www.xuanxiadetox.com/>

May I quote from it extensively in my written coursework? You have MUCH to offer the public in this regard. You have done important work.

Sincerely,

Harvey Kaltsas

Dear Harvey,

Thank you so much for contacting me! I am truly honored that you found my website useful and would like to use the information for a course you're putting together. You are more than welcome to reference the information on the site. If you have any additional questions for me, please feel free to reach out again. I've done a fair amount of research on the subject of treating addiction and withdrawal using Traditional Chinese Medicine and have discovered that the information is not always easy to find, especially in English!

A little bit of background on what led me to this area of study: I had a friend who asked if I could help his sister get off Suboxone after having been addicted to heroin for a few years. He specifically wanted to know about Chinese herbs that could help with her withdrawal. I was at a loss. In acupuncture school we didn't learn about specific formulas to treat drug addiction beyond Chai Hu Long Gu Mu Li Tang or Ban Xia Hou Po Tang. We learned a lot about using acupuncture for addiction, especially the NADA protocol, but I didn't recall learning that much about herbs for addiction. So I started researching and discovered that there are actually a lot of modern formulas being used in China, but strangely not available here in the U.S. After sifting through various journal articles and published studies, I found that Xuan Xia Detox Formula seemed to have the most research and positive reviews behind it and had even been available in the US just a few years ago under the brand name WeiniCom. The man who was selling it was actually located not too far from where I live. He had an extensive online store selling a variety of medicinal herbs, some hallucinogenic and controversial, and some like WeiniCom, that had banned herbs in them. The FDA eventually found out about his operation and shut him down.

Knowing that I couldn't get a hold of the original WeiniCom, or any of the other formulas I was discovering, I decided to try and recreate the formula without the banned herbs. I found two different recipes for Xuan Xia Detox Formula and combined them, replaced the Ephedra and Nauclea spp., and wrote my own dosages since I was never able to track down the actual amounts of each herb in the formula.

I haven't gone so far as manufacturing the formula, as I was unsure if the original manufacturer held any patents on it here in the U.S. But because there is a need for these kinds of formulas within our current opiate epidemic, I decided to try and make this formula and a few others available to the public. Although I sell the formula from my website, I am providing it to people as an herbal prescription, prescribed individually to each member-patient. This way I can also modify the formulas based on patients' specific needs and conditions. Back to the original story of my friend's sister - she was the first to try my version of Xuan Xia and after two bottles she was successful in weaning herself off the Suboxone. She's been clean ever since. If it hadn't worked so well for her I probably wouldn't have pursued making the formula available to others.

Through my studies I found a few other formulas that were relatively easy to prepare or modify and have those available on my website as well (see Fu-Yuan Pellet, U'finer Capsule, and Heantos). I believe these and other addiction formulas are not available here in the U.S. because they tend to contain banned herbs, endangered animal products, and likely make health claims on the label. Tai Kang Ning, for example, had so many banned herbs in it that I couldn't re-write it and end up with a similar formula - it would have been something completely different. But I was able to track down the recipe for it. A friend of mine recently went to China and I asked him to try and track down as much information as he could about addiction/withdrawal formulas that are being used there. I even bribed him to try and bring me back a few bottles if possible! Really, I just want to see the herbs and dosages since these are so hard to track down even in the published studies. I'll let you know if I get anymore good information from him.

I've had other researchers and manufacturers contact me about these formulas and their own withdrawal products being used in Thailand, Malaysia and Vietnam, but unfortunately I'm not able to really help them since I am not manufacturing the herbs myself. I am interested in possibly doing that in the future, but I admit it's not an area that I'm familiar with. I know that there are several addiction/withdrawal products currently on the market in the U.S. using Western herbs and supplements, but you never see these on retail shelves. They are usually only available online. If you or someone you know is knowledgeable in navigating FDA guidelines and patents for herbal supplements, I'm definitely interested in learning more. For me, it's all about making these products accessible because SO many people need them. I thank you again for reaching out because I know through your course you will be educating practitioners about this important area of our medicine that most of us lack the training in. Do let me know if I can be of any more help, and also when your CEU course is finished and available. I will probably want to take it!

Sincerely, Lauren Laks, L.Ac., MSTCM

B. Lauren Lak's Treatment Plan for Opioid Addictions

“Take everything with easy to digest foods, such as soups and stews, except for probiotics, which should be taken on an empty stomach. Drink lots of fluids (water, tea and natural juice preferred). If anything causes stomach upset, reduce dosage until symptoms resolve.

1. Modified Xuan Xia – 3 caps every 3 hours as needed for pain and fatigue; not to exceed 15 caps in one day; reduce dosage to 2 caps 3 times daily after symptoms reduce; reduce dosage to 1-2 cap servings if formula causes stomach upset OR Chai Hu Jia Long Mu Tang + Yan Hu Suo / Corydalis – same dosing as Modified Xuan Xia and Yan Hu Suo listed below
2. Black Cumin Seed Oil – by Life Extension, follow dosing on label
3. Yan Hu Suo / Corydalis – to be added if symptoms are severe; 1 cap 3 times daily
4. Da Huang / Rhubarb Root – only to be taken if there is constipation, 1 cap 3 times daily until bowel movement
5. Asafoetida – 450-900 mg caps, to be added if symptoms persist after 10 days; follow dosing on label
6. Ban Xia Hou Po Tang – to be used if there is extreme restlessness or insomnia, 3 caps 3 times daily
7. Magnesium – Natural Vitality, Natural CALM Magnesium Powder, for muscle spasms, restlessness, insomnia, and/or constipation, follow dosing on label
8. Multivitamin – Whole Foods Brand High Potency One-A-Day, 1 tablet daily with food
9. Amino Acid Complex – Super Balanced Neurotransmitter Complex and/or Mood Sync by Pain and Stress Center, follow dosing on label
10. Omega Oil Blend – Udo's Oil, 3-6-9 Blend, 180 caps, follow dosing on label
11. Probiotics – RenewLife Critical Care 50 billion; 1 cap daily on an empty stomach
12. Ear Seeds – place seeds on the ear points shown in the diagram (Neurogate, Sympathetic, Relax Muscles, Liver, Kidney, and Subcortex); can be worn several days in a row before adhesive comes off. Place 5 points in each ear, rub each point/seed several times a day esp. when symptoms are strong. The stronger the stimulation on the ear seed, the better the response. Use tweezers to place and remove.
13. Community Acupuncture – try to get community acupuncture treatments daily or several times a week especially for the first 2 weeks. Acupuncturist may be able to place ear seeds for you too. Private acupuncture is also good, but is generally more expensive, especially if you get multiple treatments per week."

C. TCM Herbal Protocols from the Website of Lauren Laks, L.Ac., MSTCM - <https://www.xuanxiadeto.com/>

Editor's Note: This entire C. section is excerpted directly from Lauren's website
<https://www.xuanxiadeto.com/>

Chinese herbal therapy has been used to treat opium dependence since the Ming and Qing Dynasties when opium was imported to China. Xuan Xia Detox Formula (also known as WeiniCom, *Xuan Xia Qudu Jiaonang*, or Xuan Xia Detoxification/Detoxification Capsules) is an herbal formula used to help those detoxing off of opiates (like codeine or morphine), synthetic opioids (like heroin, methadone, suboxone, oxycodone, or fentanyl) and other addictive substances. It's one of the top studied Chinese herbal formulas to help with addiction and its associated withdrawal symptoms.

Useful for withdrawal from:

- Heroin
- Oxycodone
- Fentanyl
- Codeine
- Morphine
- Methadone
- Suboxone
- Painkillers
- Street Drugs
- Alcohol
- Tobacco
- Nicotine
- Caffeine

From the original manufacturer:

"WeiniCom is a powerful, all natural detoxification treatment for those suffering from drug, alcohol & smoking addiction. This ancient formula detoxifies the body and reduces the severity of withdrawal symptoms. Most users will feel complete relief after only 12 - 15 days.

"It is a perfectly balanced herbal formula that is based upon a 200 year-old Traditional Medicine used to combat addictions of all types.

"WeiniCom is non-narcotic, non-addictive, pharmaceutical free and is generally well tolerated when compared to conventional western."

Ingredients

Our [Lauren's] version of Xuan Xia Detox Formula is different/modified from the original formula offered in China and imported into the United States a number of years ago. That

formula had several herbs that are now illegal or hard to import into the United States, such as Ephedra (a stimulant) and Nauclea spp. (which was found to be contaminated with Tramadol either purposefully or indirectly, such as from water run-off from nearby livestock farms.) Some versions of WeiniCom contain the potentially addictive herb, Kratom (*Mitragyna speciosa*), and the toxic herb Yang Jin Hua (*Flos Daturae*). Our version does not contain these controversial herbs.

Xuan Xia Detox Formula (Modified) only contains legal herbs - each one chosen for different aspects of addiction withdrawal. We have added replacements for the herbs that had to be left out and also added some herbs that are well-known or backed by clinical studies to help with withdrawal symptoms.

Ingredients: Proprietary Blend -

- Yan Hu Suo
- Dang Shen
- Wu Jia Shen (Ci Wu Jia)
- Ling Zhi (Hong)
- Sheng Jiang
- Huang Qi (Bei)
- Hou Po
- Hong Jing
- Mo Yao (Duan)
- Chuan Xiong
- Ren Shen (Hong)
- Ru Xiang (Duan)
- Tian Ma
- Gan Cao
- He Zi
- Huang Lian (Chuan)
- Wu Wei Zi
- Dong Chong Xia Cao (CM)
- Yin Yang Huo, Da Zao (Hong)
- Xi Yang Shen

5:1 concentrated water-extract granules

Carrier: Dextrin (derived from non-GMO corn)

114 grams / capsules

Here is a breakdown of the herbs in the formula and their traditional uses:

“Yan hu suo (*Corydalis yanhushuo*) - *Corydalis*: perhaps the most important ingredient, used for pain relief, sometimes used alone for addiction - strongly moves blood and stops pain

Dang shen (*Radix Codonopsis*) - boosts energy, replenishes fluids lost from vomiting

Ci wu jia (*Eleutherococcus senticosus*) – Siberian Ginseng - boosts energy, moves blood, stops pain, sedative

Ling zhi (*Ganoderma Lucidum*) – Reishi Mushroom - strong sedative

Sheng jiang (Zingiber officinalis) – Ginger (fresh) - aids digestion, stops vomiting, reduces toxicity

Huang qi (Astragalus membranaceus) - Astragalus - strongly boosts energy, improves immune function

Dang gui (Angelica sinensis) - Angelica - strengthens and moves blood, stops pain, promotes bowel movements

Hou po (Magnolia officinalis) – Magnolia Bark - stops vomiting and diarrhea, sedative commonly used for addiction

Hong jing tian (Rhodiola crenulata) - Rhodiola - adaptogenic herb, helps body deal with stress

Mo yao (Commiphora myrrha) - Myrrh - moves blood, stops pain, reduces inflammation

Chuan xiong (Rhizoma ligustici chuanxiong) - moves blood, stops pain, stops tremors/shaking

Ren shen (Radix ginseng) – Chinese Ginseng - strongly boosts energy, replenishes fluids lost through vomiting and diarrhea, sedative

Ru xiang (Resina olibani) - Frankincense - moves blood, stops pain, reduces toxicity, stops spasms, reduces inflammation, works in harmony with mo yao

Tian ma (Rhizoma gastrodiae) - stops spasms, stops pain

Gan cao (Radix glycyrrhizae) - Licorice - boosts energy, stops spasms, reduces toxicity

He zi (Fructus chebulae) - stops diarrhea and vomiting

Huang lian (Coptis chinensis rhizome) - Coptis - strongly cooling, stops vomiting, resolves high fever, delirium, insomnia, irritability, and disorientation, reduces toxicity

Wu wei zi (Schisandra chinensis) - Schizandra - stops diarrhea, vomiting, and excessive sweating, replenishes fluids lost through vomiting and diarrhea, sedative, improves liver function

Dong chong xia cao (Cordyceps sinensis) – Cordyceps Mushroom - strongly boosts energy, stops sweating, stops vomiting

Yin yang huo (Epimedium grandiflora) – Horny Goat Weed - boosts energy, stops pain and spasms

Da zao (Ziziphus jujube) – Chinese Black or Red Dates - boosts energy and blood, sedative, stops diarrhea and vomiting

Xi yang shen (Panax quinquefolius) – American Ginseng - boosts yin (cooling energy), clears deficiency heat

“Some interesting points to note about the formula:

- Corydalis is the chief herb for relieving pain and withdrawal symptoms in this formula. There are many other pain relieving herbs (we call them blood movers), notably Frankincense and Myrrh - aka "Chinese aspirin." The combination of the two herbs has a synergistic effect, augmenting the pain relieving properties of each.

- There are three different types of ginseng - considered one of the most powerful herbs to restore vitality. Ginseng is highly revered in Chinese medicine because it is considered a life-saving herb - so the formula can literally bring an addict back to life!

- There are a number of adaptogenic herbs - herbs used to relieve the ill-effects of stress and rewire how our body responds to stress. These include the ginsengs, reishi mushroom, astragalus, cordyceps mushroom, and rhodiola.
- There are a number of herbs specifically to stop vomiting, diarrhea, and shaking, and to replenish the fluids that are lost during extreme withdrawal.
- There are a number of sedative herbs in the formula, as well as a number of tonic herbs (energy-boosting). These are two herb groups with opposing actions, yet when they are combined they can treat the ups and downs of withdrawal - from extreme fatigue, depression, chills, to irritability, insomnia, pain, vomiting, etc.
- There are a few herbs to decrease toxicity as addicts are detoxing off medication or drugs that are toxic to the body, especially at high levels and when taken long term.

CAUTIONS & CONTRAINDICATIONS

Certain people should be cautious taking this formula. Please consult with your healthcare provider before starting this formula if:

- you are taking blood thinners
- you have high blood pressure
- you have heart, kidney or liver problems
- you are taking steroid medications
- you are pregnant or breastfeeding

WARNING: Anybody attempting to abruptly or gradually stop taking drugs, alcohol or prescription medications should be under the supervision of a qualified medical doctor. Please do not attempt to detox alone or outside of a medical detoxification program.

DOSAGE INFORMATION

This 114 gram formula, which comes out to approximately 285 capsules, is intended to last for a typical detox period of 10 days, with a maximum dosage of 10 grams per day. Some patients will require less than 10 grams per day and the formula will last longer. The exact dosage for each individual will vary based on age, height/weight and sensitivity to herbs. The following instructions are provided to help determine your individual dosage requirement.

Recommended Dosage: 5 capsules every 3 hours as needed, not to exceed 10 grams per 24 hours (approx. 25 caps). Take each dose with a full glass of preferably warm water. Reduce dosage if formula causes stomach upset and try taking with food.

Some studies have shown that Chinese herbs are most effective after the first 3 days of withdrawal. For this reason, it may be more beneficial to begin taking this formula 3 days prior to planned withdrawal.

Alternate Dosing (from the original manufacturer):

Days 1 - 3: 5-6 capsules, 3 times daily.

Days 4 - 7: 3-4 capsules, 4 times daily.

Days 8 - 15: 3 capsules, 2 times daily.

"Begin taking this product as directed 4 hours before unpleasant symptoms are expected to occur. To maximize the effectiveness of this product, continue taking as directed for 16 full days. It may be necessary to continue taking 2 capsules daily to achieve the desired results."

This formula can be taken long-term for on-going support and prevention of PAWS (post-acute withdrawal symptoms).

D. Research on the safety and efficacy of TCM Herbal Remedies for Opioid Addiction

[Editor's Note: The commentary and research in this section was provided by Lauren Laks, L. Ac., MSTCM and is excerpted directly from her website

<https://www.xuanxiadetox.com/>]

People often wonder about the safety and effectiveness of using Xuan Xia Detox Formula (aka WeiniCom) for treating their withdrawal symptoms. Fortunately, there is a good amount of research done on this subject. The following excerpts are taken from a variety of published studies on using herbal therapy in the treatment of addiction and withdrawal. Some of the studies focus on the specific herbs used in Xuan Xia Detox Formula, while others focus more on using Chinese Herbal Therapy in general. Different types of addiction are addressed.

[Journal of Psychoactive Drugs](#)

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A Comparative Clinical Study of the Effect of WeiniCom, a Chinese Herbal Compound, on Alleviation of Withdrawal Symptoms and Craving for Heroin in Detoxification Treatment

Wei Hao & Min Zhao

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- <http://dx.doi.org/10.1080/02791072.2000.10400450>

Abstract

WeiniCom is a Chinese herbal compound. The purposes of this double blind study were to evaluate (1) the efficacy of WeiniCom in reducing acute opioid withdrawal symptoms and craving, and (2) the side effects of WeiniCom, in each instance by comparing WeiniCom with buprenorphine, an established opioid detoxification treatment agent. Forty-two heroin addicts meeting the criteria of dependence in DSM-IV were randomly assigned to two treatment groups: a WeiniCom group (21 cases), and a buprenorphine group (21 cases). The Withdrawal Symptom Rating Scale and the Craving Rating Scale were employed to assess acute withdrawal symptoms and craving for heroin, and the Side Effects Rating Scale was used to measure side effects in the 14-treatment period. Both the WeiniCom and buprenorphine treatments are well-tolerated and very safe. Overall, the relief from opioid withdrawal symptoms and craving was better in the WeiniCom group than in the buprenorphine group. The rate of reduction in the severity of the withdrawal symptoms was faster in the WeiniCom group than in the buprenorphine group. By day nine to 10, the WeiniCom group showed very few withdrawal symptoms. In contrast, from day five on, the buprenorphine group continued to report relatively high scores for withdrawal symptoms and craving. WeiniCom demonstrated positive effects quickly, and required a shorter treatment period to achieve a desired degree of elimination of acute withdrawal symptoms and craving.

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Herbal Medicines for the Management of Opioid Addiction Safe and Effective Alternatives to Conventional Pharmacotherapy?

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4. Chinese Herbal Remedies

Opioid abuse and addiction have been a public health hazard in China for much of the last 200 years. Governmental policies enacted in the 1950s curtailed opioid abuse, but economic reforms of the 1980s led to a widespread resurgence of heroin addiction. To confront the growing problem of drug addiction, the Chinese government has initiated pharmacotherapy programmes based on Western addiction treatment protocols. Unfortunately, the predominant treatment for opioid addiction is short-term detoxification with methadone or buprenorphine at compulsory reeducation through-work centres. These programmes have faced great difficulties. Treatment centres are underfunded, and because patients undergo forced detoxification, they have high rates of relapse and low rates of recovery. Finally, many opioid addicts live in rural areas, where the reach of treatment programmes is limited.

Traditional Chinese medicines have therefore received considerable interest as potentially more acceptable and less costly alternatives to standard pharmacotherapy. The Chinese State Food and Drug Administration has approved at least ten herbal-based products for the treatment of opioid withdrawal, with several more in clinical trials. Although Asian herbal remedies are often mixtures of plant matter, animal material and, in some cases, minerals or even toxic metals, the use of specific components in these complex mixtures as treatment for opioid withdrawal is supported by preclinical and clinical data.

Corydalis yanhusuo is a herbal analgesic with sedative, hypnotic and antihypertensive properties. The active component, the natural product levotetrahydropalmatine (1-THP), inhibits in a murine model the locomotor hyperactivity induced by oxycodone. In addition, treatment with 1-THP can attenuate morphine-induced withdrawal syndromes and conditioned place preference in mice.

Ginseng is another botanical commonly used in Chinese traditional remedies. Two major types of ginseng exist, *Panax ginseng* (Asian ginseng) and *Panax quinquefolium* (American ginseng). The main active natural products in *Panax ginseng* are called ginsenosides, of which more than 20 have been characterized. Ginsenosides have putative effects on the CNS and cardiovascular system, and may alter metabolism and immune function. *Panax ginseng* attenuates the physiological effects of drugs of abuse including morphine in pre-clinical studies. A multicentre clinical trial found that Radix ginseng (the root of *Panax ginseng*) was safe and effective for the treatment of moderate-to-severe acute heroin withdrawal. In this double-blind study, 212 heroin addicts were randomized to treatment with either the ginseng herbal mixture or to lofexidine over a 10-day period. The investigators found that the herbal mixture was as effective as lofexidine at alleviating the symptoms of opioid withdrawal, with patients reporting only gradual improvement in symptomatology over the study period.

The active chemical in *Panax quinquefolium*, not found in *Panax ginseng*, is pseudoginsenoside-FII (PFII), a saponin. *Panax quinquefolium*, especially PFII, exerts distinct effects following morphine administration. PFII attenuates memory impairment in the Morris water maze test, analgesia measured by tail pinch, locomotor sensitization and, at higher doses, the expression of conditioned place preference. Neurochemically, PFII antagonizes opioid receptor signalling and decreases the concentrations of dopamine and its metabolites in the brain of test animals treated with morphine.

Although the side-effect profile of traditional Chinese remedies is often unreported, the low incidence of adverse effects compared with lofexidine suggests that they are safe to use."

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A Comparative Clinical Study of the Effects of the Traditional Chinese Medicine Jinniu Capsules and Lofexidine on Acute Heroin Withdrawal Symptoms

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"Radix ginseng extract pseudoginsenoside-F11 decreased morphine-induced behavioral sensitization and extracellular glutamate levels in the medial prefrontal cortex in mice (12), and ginsenosides Rg1 inhibited morphine induced conditioned place-preference (13, 14). The main component of corydalis, levotetrahydropalmatine (L-THP), attenuated drug-induced reinstatement of cocaine seeking (15). L-THP also ameliorated opiate craving and increased the abstinence rate in heroin abusers (16)."

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Traditional Chinese medicine in treatment of opiate addiction 1

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Chinese medicine in the treatment of opiate addiction

Currently, the SFDA has issued approval of 10 Chinese medicines for use in clinical practice for the treatment of addiction, including the Fukang tablet, Lingyi capsule, Yian Liquid, Jitai tablet, Fuzhengkang granule, Anjunning mini pill, Kangfuxin, Xuanxia detoxification capsule, Shifusheng capsule and Zhengtongning granule for opiate acute detoxification [9-11] . Clinical trials of 6 Chinese medicines are currently underway and pending approval by the SFDA. These include the Taikangning capsule, Jiedukang capsule, Yanshen liquid, Fuyuan granule, Jingan Jiedu pill, Jinjiawang granule and Junfukang capsule. Several additional Chinese medicines are undergoing preclinical trials.

Chinese medicines act by targeting multiple processes in the human body. Some papaveraceae herbs have been used in traditional prescriptions, such as *Rhizoma corydalis* (yanhusuo), *Flos daturae*, *Semen hyoscyami*, *Herba chelidonii*, and snake venom for pain relief [12] , *Radix ginseng*, *Radix astragali*, *Radix panacis quinquefolii*, *Radix aconite lateralis praeparata*, *Radix angelicae sinensis* and *Cordyceps* for healthy Qi reinforcement, *Rhizoma pinelliae*, *Semen ziziphi spinosae*, *Radix polygalae* for sedation and tranquilization, *Flos lonicerae japonicae*, *Herba taraxaci*, *Gossampinus malabarica* (mumian), pumpkin, *Radix glycyrrhizae*, pine leaves, small flower milkwort herbs with roots (*Jinniucuo*), and *Hedyotis diffusa* (*baihua sheshecao*) for body toxin-removing [13–15] . The treatment effects of these herbs show synergy when used in combination.

Patients with opiate dependence usually experience withdrawal symptoms from day 1 to day 4 following Chinese medicine administration. Chinese medicine is not as effective as methadone, but most residual symptoms are tolerable. Sometimes tranquilizers are required as a supplement. Therefore, TCM treatment should start in advance or as early as possible to control withdrawal symptoms if it is used without other medicines. For drug users with severe opiate dependence and symptoms (eg those with a long history, high dose and long term IV drug users), treatment with only Chinese medicine is inadequate. It is recommended that low-dose, narcotic detoxification drugs, such as methadone or buprenorphine be co-administered together with Chinese medicine. Usually, low-dose, narcotic detoxification drugs are administered from day 1 through to day 5 so that the fast action of the narcotics and the non-dependent long-lasting effects of the Chinese medicine can complement each other. Most Chinese medicines could be used at a low dosage for long-term treatment with the aim of controlling protracted withdrawal symptoms for rehabilitation and for preventing relapse. Generally, Chinese medicines are safe; most have no obvious side effects on respiration, blood pressure, heart rate and liver and kidney functions. Some patients may suffer from a stomach upset, nausea, vomiting and diarrhea, dry mouth, blurred vision, loss of balance, somnolence and dizziness, but most do not require treatment. Usually, symptoms disappear after dose decrement or after subsequent treatment.

Previously published studies indicate that most Chinese medicines have the following characteristics: (1) sedation, pain relief, local anaesthesia, hypnosis and anti-convulsion; (2) stabilization of blood sugar, improvement of protein metabolism, protection of liver, blood pressure control and anti-hypoxemia; (3) anti-fatigue, anti-stress and anti-shock; and (4) cardiovascular system protection and modulation of immune function. For example, *Radix aconite* (*fuzi*) is effective in relieving body reeling and head and extremities tremble in opiate withdrawal of rats. *Radix ginseng* is effective in preventing morphine tolerance, addiction and adaptation in the regulation of body functions and in relieving withdrawal symptoms [16]. *Rhizoma* (*yanhusuo*) can control nervous vomiting, dilate the coronary artery, antagonize arrhythmia and regulate the function of the GI tract [17] .

In addition, ginseng total saponin inhibits the development of reverse tolerance to the ambulatory accelerating effects of morphine and prevents the development of dopamine receptor supersensitivity induced by the chronic administration of morphine [43]. Pseudoginsenoside-F₁₁ inhibits the conditioned place preference induced by morphine in mice [44]. L-tetrahydropalmatine, an active component of *Corydalis yanhusuo*, can attenuate the locomotor-stimulating effects of oxycodone (an opiate receptor agonist) and inhibit the development and expression of oxycodone behavioral sensitization [38]. In recent studies, L-tetrahydropalmatine was found to inhibit physical dependence in morphine-dependent mice and significantly reduce the development of the conditional place preference induced by morphine in mice [45,46].

TCM may have an advantage in the rehabilitation and prevention of a relapse of opiate addiction. Prevention of drug relapse and completion of rehabilitation is a critical aspect in the treatment for addiction. There are many TCM which may aid in rehabilitation. For example, ginseng enhances immune function and metabolism and possesses anti-stress and anti-aging activities. Several ginsenosides were proven to be non-organ-specific tumor suppressors and improved learning and memory in patients with Alzheimer's disease [52]. More than 28 ginsenosides have been extracted from ginseng, and might be associated with a wide range of therapeutic actions in the central nervous system and cardiovascular and endocrine systems [53]."

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REVIEW ARTICLE

Traditional Medicine in the Treatment of Drug Addiction

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"HERBAL MEDICINE IN THE TREATMENT OF DRUG ADDICTION

Ginseng

There are two major types of ginseng, *Panax ginseng* (Asian ginseng) and *Panax quinquefolium* (American ginseng). *Panax ginseng* is a well-known Chinese traditional herbal medicine. It has been used for hundreds of years in China and later gained popularity in the West. *Panax ginseng* has been demonstrated to have a profound impact on the central nervous and cardiovascular systems, and it promotes endocrine secretions effecting immune function and metabolism (10). The main active compounds in *Panax ginseng* are called ginsenosides; more than twenty ginsenosides have been isolated, including Rb, Rc, Re, and Rg (11). The active

chemical in *Panax quinquefolium* is Pseudoginsenoside-F11(PF11), an ocotillol-type saponin; this does not exist in *Panax ginseng* (12).

Panax ginseng has been demonstrated to attenuate the behavioral effects of drugs of abuse including morphine, methamphetamine, cocaine, and alcohol in both pre-clinical and clinical studies (13). For example, ginsenosides substantially inhibited conditioned place preference induced by methamphetamine (14) or cocaine (15). Further, ginsenosides significantly attenuated the withdrawal syndromes precipitated by naloxone in morphine-dependent mice (16), and inhibited the conditioned place preference and hyperactivity induced by morphine (17). Unfortunately, *Panax ginseng*'s effects have not been examined in the animal model of drug self-administration, which makes it impossible to draw a definitive conclusion on *Panax ginseng*'s ability to inhibit voluntary drug intake.

Ginseng's inhibitory effect on various drugs of abuse appears to be associated with modulation of dopaminergic transmission. Administration of the *Panax ginseng* extract, ginseng total saponin, can substantially attenuate ambulatory hyperactivity to apomorphine in mice that had repeated exposure to nicotine (18). This finding suggests that ginseng total saponin effectively inhibits post-synaptic dopamine receptor super-sensitivity in nicotine-treated mice (18). A recent study has also reported that ginseng total saponin profoundly inhibited nicotine-stimulated dopamine release in the striatum and Fos protein expression in the nucleus accumbens of mice (19). Taken together, these studies shed new light on *Panax ginseng* as a potentially useful therapeutic agent for the treatment of drug addiction.

Panax quinquefolium, especially PF11, has a different range of effects on drugs of abuse, particularly methamphetamine and morphine. Wu et al. (20) reported that PF11 significantly attenuated the behavioral effects of methamphetamine including anxiety-like behavior in the light-dark box task, increased latency and error counts in the forced swimming task, and prolonged escape latency in the Morris water maze task. Li et al. (21) reported that PF11 significantly inhibited four major effects of morphine: 1) memory impairment in the Morris water maze test, 2) expression of conditioned place preference (at a higher PF11 dose), 3) analgesia tested by tail pinch, and 4) the development of locomotor sensitization. Neurochemical studies have demonstrated that PF11 antagonizes morphine-stimulated opioid receptor signaling (22) and decreases the concentrations of dopamine and its metabolites in the brain of morphine-treated animals (20). These results suggest that PF11 could reduce relapse in methamphetamine and opiate dependence and protect against methamphetamine-induced neurotoxicity from excessive brain dopamine levels.

Corydalis Yanhusuo

Corydalis yanhusuo is a Chinese traditional analgesic that has sedative, hypnotic, and antihypertensive properties (57). Levotetrahydropalmatine (L-THP) is its primary active chemical, and L-THP in mice inhibits the hyperactivity induced by oxycodone, an opioid receptor agonist similar to morphine (102). In addition, treatment with L-THP can attenuate morphine-induced withdrawal syndromes (103) and conditioned place preference in mice (104). L-THP dose-dependently reduces cocaine self administration and attenuates cocaine-induced reinstatement and locomotor activity (105). Supporting these promising preclinical findings, a clinical trial conducted in China found that L-THP effectively reduced drug craving, withdrawal syndromes, and relapse rates in recovering heroin-dependent patients (19). Thus, *Corydalis yanhusuo* may become an effective pharmacotherapy for drug abuse and dependence.

The neurochemical mechanism for l-THP's anti-addictive properties may be antagonism of dopamine transmission. Levotetrahydropalmatine inhibits dopamine D1 and D2 receptors and acts on the nigra-striatal neuronal pathways to inhibit both pre and post-synaptic receptors (106); (107). Electroacupuncture induced analgesia can be enhanced by l-THP presumably via the selective inhibition of dopamine D1 receptors (108). However, l-THP also prevents inhibition of L-type Ca²⁺ channels (106), and inhibition of the L-type Ca²⁺ channel is essential for the development of morphine tolerance, dependence, and sensitization. Thus, l-THP could attenuate morphine-induced neural and behavioral plasticity via the blockade of L-type Ca²⁺ channels (109, 110). Finally, pre treatment with l-THP inhibits several of these neuronal changes associated with addictive drugs making it an excellent candidate medication for "re-normalization" of brain function that can be disrupted by chronic drug dependence (20)."

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A Study on Fu-Yuan Pellet, a Traditional Chinese Medicine Formula for Detoxification of Heroin Addictions

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"Some studies reported that the dopamine-2 receptor plays an important role in morphine addiction (9). It was concluded that D2 dopaminergic receptors may play a role in the expression and development of tolerance to the antinociceptive effect of morphine. Rotundine is 1-optical isomer of tetrahydropalmatine, which is an active alkaloid isolated from the stem tubers of the Chinese medicinal herb, *Corydalis Rhizoma* (10), and found to have analgesic, sedative and tranquilizing effects. The biochemical studies proved that rotundine was a dopamine-2 receptor blocker (11, 12). The binding study revealed that the affinity of rotundine toward dopamine-2 receptors was 211 times higher than that toward dopamine-1 receptors (13). Therefore, the mechanism of rotundine inhibiting morphine induced psychic dependence may involve the dopamine-2 receptor. Also, *Corydalis Rhizoma* can control nervous vomiting, dilate the coronary artery, antagonize arrhythmia, and regulate the function of the GI tract (14). In recent studies, l-tetrahydropalmatine can inhibit the rewarding effect induced by morphine and may play a role in the treatment of morphine addiction (15)."

A Database on Traditional Chinese Medicine Treatment for Drug Addiction

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"3.3 Herbal analysis

3.3.1 Commonly used herbal function categories

The results indicated that more than 200 Chinese herbs were reported in 150 original research literatures and 85 patent files. These herbs had a very broad functional spectrum, and might be classified into 23 functional categories according to the classification system of Chinese herbal medicine. The top five function categories were tonifying herbs, herbs for promoting blood circulation and removing blood stasis, herbs for clearing away heat, herbs for tranquilising the mind and herbs for exterior syndrome.

3.3.2 Commonly used herbs

In 150 original research literatures and 85 patent literatures, the top ten kinds of the most frequently used herbs were Radix Glycyrrhizae (Gancao), Poria (Fuling), Rhizoma Corydalis (Yanhusuo), Radix Angelicae Sinensis (Danggui), Radix Ginseng (Renshen), Radix Astragali (Huangqi), Rhizoma Atractylodis Macrocephalae (Baizhu), Semen Zizyphi Spinosae (Suanzaoren), Radix Polygalae (Yuanzhi) and Flos Daturae (Yangjinhua).

4. Discussion

Based on an extensive search and collection, a most comprehensive and updated bilingual database (CDR) on TCM treatment for drug addiction has been established, which contains 340 professional literatures including 85 patent files. The results of literature categorisation and classification showed a significant increase of publications on clinical and laboratory researches in the recent years. This reflected that the clinical application and experimental research of TCM in drug detoxification and rehabilitation gained popularity, and the quality of research data was also improved gradually.

For systematic search of related literatures in this project, we had screened various Chinese databases by our well-designed searching strategy. A total of 141 and of 99 non-overlapping related literatures were found in the Database of Chinese Science Journals and CBMDisc respectively. These results indicated that large scale integrated databases could only provide part of related literatures, of which the data proportion was below 50% of our total collections. Some scholars (Zhan, 2002) pointed out that multi-discipline databases could only provide approximately 2/5 of literatures in a specific domain; and “grey literatures” such as conference theses, degree theses, patent files and also drug development research reports were far more difficult to be accessed through general databases. Therefore, our computerised, 392 bilingual (Chinese–English) database on TCM treatment for drug addiction is non-replaceable in professional application value so far. In order to maximise the utility of this database, we suggest updating it every three years.

Almost all published data from Mainland China as well as other countries claimed that TCM including Chinese herbal therapy (CHT), acupuncture therapy and Qi-gong therapy might be potential ways for treatment of drug addiction. CHT was the most commonly used therapy for drug detoxification in the published literatures collected by our database. Based on data analysis in this study, the five function categories of Chinese herbs and the ten Chinese herbs were identified as the most commonly used herbal medicine for drug detoxification. It will be valuable to perform further pharmacological experiments and clinical trials on the efficacy of these herbs for obtaining direct evidence.

According to TCM theories, the clinical manifestations of drug addicts mostly belong to the “deficiency syndrome”. Even though they may have “excessive symptoms”, it is most probably “asthenia in pathogenesis but sthenia in manifestations”. Our analysis indicated that tonifying herb was the top one of the five frequently used herbs in functional categorisation; and among

the ten most frequently used herbs, Radix Glycyrrhizae (Gancao), Radix Angelicae Sinensis (Danggui), Radix Ginseng (Renshen), Radix Astragali (Huangqi) and Rhizoma Atractylodis Macrocephalae (Baizhu) are typical tonifying herbs. These findings matched the understanding and the therapeutical principles of TCM theories. Contemporary pharmacological researches proved that many tonifying herbs exerted significant regulatory effects on the neuroendocrine system and immune system (Hou, 2002). This can be a pharmacological foundation for exploring efficacy of herbal treatment for drug addiction.

It is well known that the withdrawal syndrome during acute detoxification can be controlled rapidly by different therapies, but to overcome the protracted abstinence syndrome that is closely related to the relapse rate in patients has been one of the unsolved problems. Some Chinese papers have reported a beneficial effect of herbal therapy on longer-term protracted abstinence syndrome during rehabilitation period (Zhang & Zhou, 1995; Mo et al., 2002). The efficacy and safety of CHT on treatment of protracted abstinence syndrome deserve further confirmation by long-term clinical trials."

Meta-analysis on Chinese Herbal Therapy for Heroin Withdrawal Syndrome

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4. Discussion

Evidence-based medicine can provide the highest standard evidence (current best evidence) for clinical application. In terms of principles and measurements of evidence-based medicine, systematic review is an evidence-based qualitative process of defining the questions, searching literatures, assessing the quality of trials, applying eligibility criteria, examining and comparing the results of eligible trials, and conducting statistical synthesis of the data. Meta-analysis may be a part of a systematic review when individual trials are similar with each other and can be integrated for further estimate by which the data are combined statistically to yield a quantitative analysis on the size of the treatment effect and a test of homogeneity in the estimate of effect size.

In this study the results of meta-analysis indicated that CHT was able to ameliorate the signs and symptoms of heroin withdrawal. A comparison on the therapeutic effects of 11 included trials supported that CHT might be more advantageous than Western medications (clonidine, methadone, tramadol, estazolam and buprenorphine) for detoxification of heroin addicts. Interestingly, a comparison between CHT and clonidine was further conducted by a subgroup meta-analysis, and the combined effects of 5 trials with homogeneity provided power evidence that showed statistically significantly positive benefits from CHT treatment. Although the data from this meta-analysis point towards CHT and methadone have similar effects in management of heroin withdrawal, there are limited data available from clinical trials for comparing CHT with methadone, tramadol, estazolam, buprenorphine and other western medications so far.

Despite the number of eligible trials and sample size of the trials are significantly insufficient for quantitatively assessing some aspects of CHT treatment by means of meta-analysis, additional evidences on the efficacy of CHT can be obtained from the results of many observational trials while some statistical form of controls has addressed alternative explanations of apparent effectiveness. These large scales of observational trials have generally supported the results

from randomized controlled clinical trials and this systematic review that showed a significant therapeutic effect of CHT in treating heroin withdrawal syndrome.

The basic form of herbal medicine applied in the included 11 trials is herbal formula which is prepared Part 5: Advances in drug abuse research 381 as herbal capsule, tablet, powder or decoction. Each herbal formula is composed of different kinds of natural herbs that contain very complex effective components such as polysaccharides, alkaloids, cholines, flavones, isoflavones, coumarins, lignins, amino acids, fatty acids, vitamins and so on. These herbal components exert broad and significant effects on regulating neuroendocrine system and immune system, and improving substance and energy metabolism in the body. It is presumed that the main role pattern and pharmacological mechanism of herbal therapy should be multi-target regulation and rehabilitation that may be laid a firm foundation for the application of CHT in heroin detoxification.

According to theories and experiences of traditional Chinese medicine, the main principles and methods of treatment of heroin withdrawal syndrome with CHT include: (1) removing toxic materials from the body by emetic therapy, purgative therapy, diuretic therapy (inducing a mild and temporary vomiting or diarrhea or diuresis) and detoxification therapy (improving the metabolism of drugs), (2) relieving symptoms (stopping pain and vomiting, improving digestion, treating restlessness and insomnia, etc.), and (3) invigorating the body functions. In recent years, many traditional therapies and herbal medicines have been systematically verified on their practice values by modern biomedical techniques. It should be notable that amongst other systematic reviews including meta-analyses on Western medications such as clonidine and methadone conducted so far, the combined effect size usually focused on relative risk of retention rate, reduction of heroin use and criminal activity etc. is different to the outcome measurement of this review. Rather than assessing the patient number whose heroin withdrawal syndrome was treated effectively, we proposed in this review to investigate effects of CHT by other indexes which were commonly concerned by clinical practitioners. The assessment should be on intensity of withdrawal by withdrawal syndrome scores, time-course of withdrawal or duration of treatment, predominant signs and symptoms, drug positive results in urine samples, relapse rate, and indirect indications of treatment efficacy such as criminal activities, employment status and so on. However, owing to insufficiency of data and diversity of comparison from the included trials, quantitative analysis cannot be performed for these aspects consequently. In view of the limitations of this meta-analysis by which only category data from clinical trials were assessed, further meta-analysis should be conducted on evaluation of measurement data and ranked data for verifying the findings of this study.

Our analysis also indicated that the incidence of adverse effects in patients treated with CHT was statistically significantly lower than that of Western medications. It is undoubted that the most patients received CHT may achieve a longer retention in detoxification treatment. The adverse effects reported in the patients treated with CHT were dizziness, nausea, vomiting, dry mouth, fatigue, fainting, sweating and palpitation that were generally minor in the trials. However, some herbal preparations like Fukang Pian containing toxic herbs may cause occurrence of some typical adverse effects in patients who eventually had to cease the treatment (Hu & Huang, 1995). Standard pre-clinical studies and long-term clinical trials are still lack to observe the safety of preparations of CHT."

Non-pharmacological Treatment of Addiction

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"Medicinal plants"

Medicinal plants are considered as one of the first treatment methods in alternative and Chinese medicine. On the contrary to the western medicine which prescribes a particular medication for a specific disease, in the traditional Chinese medicine, disease represents the body's imbalance or disharmony with the environment. The traditional Chinese medicine aims to help the patients as well as the organs which are under pressure. In fact, Chinese researchers have emphasized this treatment approach for a long time. Between 1840 and 1952, a large number of Chinese addicts received the traditional Chinese plants and were detoxified; however, later on it was revealed that many of these drugs included opium (Simpson 1990). Afterwards, some guidelines were approved based on the researches conducted on the issue according to which, Food and Drug Administration of China inhibited using opium containing drugs in addiction treatment centers. Based on the new guidelines, using the following 10 drugs was allowed and considered beneficent in treatment of addiction: Ganciao, Poria, Yanhusuo, Danggui, Renshen, Huangqi, Baizhu, Suanzaoren, Yuanzhi, and Yangjinhua (Min 2007). Considering the categorization of Chinese medicine which is based on a unique theory, strengthens health through vital energy, and removes the effect of the toxic materials, these plants are effective in treatment of addiction through a wide range of functions. These plants have different mechanisms, including empowerment, improvement of blood circulation, elimination of blood stasis, removal of excess heat from the body, and peace of mind. Such plants are also used in order to remove the acute withdrawal syndrome which is similar to the conditions experienced at the beginning stages of a disease and is accompanied by symptoms, such as feeling cold, fever, headache, runny nose, and cough.

Some studies have shown that treating the addiction to opiates using Chinese herbal medicine has fewer side effects and is comparable with clonidine (Tang ET AL.2007, Xu et al.2002, Xu et al.2000, Wang et al.2004)."

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© 2006 The Authors. Journal compilation © 2006 Society for the Study of Addiction Addiction, 101, 657–665 Blackwell Science, Ltd Oxford, UKADDAAddiction0965-2140© 2006 The Authors. Journal compilation © 2006 Original Article Opiate addiction in China Yi-lang Tang et al. Correspondence to: Yi-lang Tang, Department of Human Genetics, Emory University, 615 Michael Street, Suite 301, Atlanta, GA 30322, USA. E-mail: ytang@genetics.emory.edu. Submitted 14 January 2005; initial review completed 27 May 2005; final version accepted 21 August 2005

REVIEW Opiate addiction in China: current situation and treatments

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"Use of Chinese traditional medicine in opiate addiction

From 1840 to 1952, traditional Chinese medicine (TCM) constituted the only standard treatment for opiate dependence, and claims for significant efficacy were often made. Practised for over 2000 years, Chinese herbal medicine is a primary component of TCM, which also includes acupuncture, dietary principles and massage, as well as therapeutic exercise and movement. In contrast to western medicine, in which specific drugs are prescribed for specific diagnoses, TCM approaches illness as the result (or manifestation) of 'imbalances' within the body, or between the body and various environmental factors. The aim of Chinese medicine is therefore to help the patient's 'stressed organ systems' to operate in a more natural, balanced state, rather than to prescribe a herbal agent to treat a particular manifestation. In China, TCM continues to be employed commonly in opiate detoxification, and in the broader treatment of illnesses including addictions. Both the Chinese government and Chinese researchers continue to place a major emphasis on this type of approach."

IV. Acupuncture Protocols for Treatment of Opioid and Other Addictions

A. Studies on the Efficacy of Acupuncture for Withdrawal from Opioids

The following meta-analysis reviews a great number of research studies on the effectiveness of acupuncture and especially of electro-acupuncture (EA) on the treatment of opioid addiction. You are invited to wade through them all, but know this: the real clinical pearls are to be found in **Section B. The Protocols Developed by Dr. Donald (Deke) Kendall** which follows this section.

Role of Acupuncture in the Treatment of Drug Addiction

From - **Complementary Therapies for the Body, Mind and Soul**

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Role of Acupuncture in the Treatment of Drug Addiction

Anfeng Xiang, Boyuan Zhang and Sheng Liu

Additional information is available at the end of the chapter <http://dx.doi.org/10.5772/60655>

Abstract

This review systematically assessed the clinical evidence for and against acupuncture as a treatment for drug addiction. The existing scientific rationale and possible mechanisms for the effectiveness of acupuncture on drug addiction were also evaluated. We used computerized literature searches in English and Chinese and examined texts written before these computerized databases existed. We also used search terms of treatment and neurobiology for drug abuse and dependence. Acupuncture showed evidence for relevant neurobiological mechanisms in the treatment of drug addiction. Although positive findings regarding the use of acupuncture to treat drug dependence have been reported by many clinical studies, the data do not allow us to make conclusions that acupuncture was an effective treatment for drug addiction, given that many studies reviewed here were hampered by small numbers of patients, insufficient reporting of randomization and allocation concealment methods, and strength of the inference. However, considering the potential of acupuncture demonstrated in the included studies, further rigorous randomized controlled trials with long follow-up are warranted.

Keywords: acupuncture, addiction, heroin, cocaine, treatment

1. Introduction

Acupuncture originated in ancient China and has been used to manage various clinical disorders for thousands of years in China. Acupuncture needles insert into acupuncture points of the body to treat many different disorders. Acupuncture needles are manipulated

manually. One of the recent technical developments was to use peripheral electrical stimulation applied via the acupuncture needles inserted into the acupoints, that is, “electroacupuncture” (EA). Currently, new methods for stimulating the acupuncture points include applying electric current to skin electrodes over the points, directing a laser light onto the points, or using finger pressure to massage selected points (acupressure). In addition, many new points and entire “microsystems” of points have been described for specific body parts, for example, scalp acupuncture and ear acupuncture (auricular acupuncture). In Western countries, acupuncture began to be known in the middle of the 1970s, yet its acceptance has increased rapidly.

Many Western patients turn to acupuncture along with conventional medical therapy to make sure they are utilizing all possible medical options. A recent survey of acupuncture released by an NIH Consensus Development Panel indicated that although there are inherent problems of design, sample amount, and appropriate controls in the acupuncture literature, extensive work has shown that acupuncture is beneficial in treating various pain syndromes, postoperative and chemotherapy- induced nausea and vomiting, some forms of bronchial asthma, headache, migraine, and female infertility. For the past 40 years, a number of studies of acupuncture applied, as a medical technique, to the treatment of heroin, alcohol, nicotine, and cocaine addictions have been reported. In light of an increasing trend in the use of acupuncture and utilization of such approaches by patients suffering from drug addiction, we intend to review the existing scientific rationale and clinical data, which indicate that acupuncture may influence the prognosis of drug addicts.

2. Acupuncture: Theory and mechanisms

It has long been a dream to cure diseases by nonpharmacological measures that activate self-healing mechanisms, without using drugs. Recent efforts along these lines were the use of vagal nerve stimulation, repetitive transcranial magnetic stimulation (rTMS), deep brain stimulation, and acupuncture to stimulate certain brain areas. Evidence presented in the present review demonstrates that it is possible to facilitate the release of certain neuropeptides in the central nervous system (CNS) by means of peripheral acupuncture point’s stimulation. In contrast to magnetic stimulation that stimulates the superficial areas of the brain (i.e., the cortex) [1], acupuncture activates various brain structures and/or the spinal cord via specific neural pathways. Any predictions made at this stage should not be overly optimistic. But the clinical efficacy demonstrated using acupuncture to ease postoperative pain [2,3], lower-back pain [4,5], and diabetic neuropathic pain [6], and the successful application of 100 Hz (but not 2 Hz) electroacupuncture for treating muscle spastic pain of spinal origin [7]E certainly hold exciting promise for the future. Gaining knowledge of therapeutic mechanisms is essential to validating therapies such as acupuncture that are difficult to test under double-blind, placebocontrolled conditions. If we try to answer the question “how the acupuncture works or what physical changes occur”, it is appropriate first to give some theoretical background for acupuncture.

Clinical treatment with acupuncture is done in light of symptom differentiation and therapeutic methods, by means of needling and moxibustion (lighted punks of artemis vulgaris) with certain manipulating methods to stimulate the selected acupuncture points for prevention and treatment of diseases. The theory of meridians and acupuncture points is the basic theory of therapy. In fact, traditional Chinese medicine is based on the concept of the flow of energy or Qi through meridian pathways in the body. Qi is postulated to flow through

196 Complementary Therapies for the Body, Mind and Soul the body in precisely located pathways or channels called meridians. These meridians are thought to be connected to various body organs as well as to each other. According to the principles of traditional Chinese medicine, illness results from an imbalance of energy flow within these meridians. Acupuncture was developed according to the principle that human bodily functions are controlled by the “meridian” and “Qi” systems. There are 365 designated acupuncture points located along these meridians. Acupuncture stimulates the points located on “meridians” along which Qi flows, breaking the blockage, and subsequently restoring the flow of energy and healthy body functioning [8].

Acupuncture points on the body have both local and systemic influences. Pain, for example, is treated not only locally but distally as well, via acupuncture points further along the meridian, drawing energy away from the pain. Conditions caused by organ dysfunction such as asthma or drug addiction are differentiated according to the specific symptoms present. Acupuncture points are then selected appropriate to both the symptoms reported and the cause of that individual’s problems.

Although different direction, angle and depth for inserting needles, stimulation intensity, such as rolling, raising, and thrusting, and Deqi may have an effect through different actions, the condition of the patient is the most important factor that influences the effectiveness of acupuncture. Numerous examples reveal that the regulatory effect of acupuncture has the characteristics of holism and bidirectional regulation. In acupuncture theory, bidirectional regulation is referred to a balancing effect of acupuncture interventions when the human body is experiencing a hyperactivity or hypoactivity due to abnormal intrinsic or external factors. The same acupuncture points’ stimulation with different manipulating techniques or stimulation parameters can regulate different functional activities of the body bidirectionally, which means to balance the functions of the body when they become hyperactive with the inhibiting effect and to restore the normal functions of the body when they become hypoactive with the exciting effect. For example, when blood pressure is too high, needling Neiguan (PC.6) can reduce high blood pressure; when blood pressure is too low, needling PC.6 can elevate blood pressure. Acupuncture-induced correction of abnormal blood pressure is observed to be dependent on the nervous, endocrinal, humoral, and dielectric regulation. Take Zusanli (ST. 36) for another example, EA at Zusanli (ST.36) can biregulate gastric activity. For gastric hypermotility, EA at ST.36 can inhibit gastric movement; but for bradygastria, EA at ST.36 can promote the peristalsis of the stomach. In addition, it is notable that some of the acupuncture points can bear special or specific curative effect on certain diseases. For example, Dazhui (GV. 14) abates fever and Zhiyin (BL.67) rectifies the position of fetus [9].

The guidance of the theory of traditional Chinese medicine is traditionally believed to be essential in achieving acupuncture’s therapeutic effect, but the metaphysical explanations may be hard to understand by modern science. In recent years, increasing research publications gave strong evidence that acupuncture could be explained on a physiological and neurobiological rather than a metaphysical basis [10, 11]. For example, in traditional Chinese medicine, the vision-related acupuncture point (VA1) (known as urinary bladder channel of BL67) is believed to be an effective acupuncture point that directly treats eye-related disorders. Various acupoints are related to corresponding specific organs rather than via the central nervous system.

Based on the knowledge of Western medicine, it is difficult to believe that acupuncture treats disorders and diseases by direct control of organs or organ-related disorders and diseases. It is known that many disorders are either controlled or affected by the brain, i.e., specific corresponding brain functional areas. Recently, Cho et al. [12] demonstrated that when acupuncture stimulation is performed at VA1 (vision-related acupuncture point), activation of occipital lobes is seen by functional magnetic resonance imaging (fMRI). Stimulation of the eye by directly using light evokes similar activation in the occipital lobes. It may represent an important step toward understanding oriental acupuncture in relationship to brain function.

In addition, the findings by Bruce Rosen of Harvard Medical School at the American Psychosomatic Society Meeting in Orlando showed that acupuncture on pain-relief points cut blood flow to key areas of the brain related with pain within seconds. Researchers applied acupuncture needles to acupuncture points on the hand linked to pain relief in traditional Chinese medicine. Blood flow decreased in certain areas of the brain, which was detected by fMRI within seconds of volunteers reporting a sense of heaviness in their hands, a sign that the acupuncture is working. The needling technique is not supposed to hurt if done correctly. When a few subjects reported pain, the MRI scanings showed an increase of blood to the same brain areas. It may provide a clear explanation to date for how the ancient acupuncture might relieve pain.

Recently, the neurophysiology of acupuncture has been investigated extensively and reviewed in detail. The principal suggestion is that acupuncture operates largely through neurotransmitters, particularly endorphin-related mechanisms. These studies demonstrate conclusively that acupuncture's effects are related to the release of a variety of neurotransmitters including natural opiates and, furthermore, that this effect is naloxone-reversible. Basic research work carried out has demonstrated that any noxious stimulus will result in endorphin release through the neurophysiological mechanism described as diffuse noxious inhibitory control (DNIC). Therefore, DNIC represents a nonspecific physiological mechanism which triggers the natural opiate system in both man and experimental animal. It has been suggested that DNIC plays a relatively minor role in acupuncture analgesia and that other systems, mediated by serotonin and noradrenaline, may be important. The mechanism of acupuncture in internal diseases, such as asthma, irritable bowel, and the treatment of symptoms such as nausea is completely unknown. Acupuncturists have hypothesized that the autonomic nervous system plays an important, but not as yet ill-defined, part in the underlying mechanisms that are involved in the treatment of such internal problems.

3. Effects of acupuncture on drug dependence

Conventional detoxification methods such as methadone and buprenorphine are effective in reducing illicit opioid use, but problems associated with their use, such as social resistance to the idea of "replacing one drug of abuse with another" and difficulties in tapering patients off the medication due to long-lasting withdrawal effects, make the search for alternative therapies important [13]. Acupuncture's utility for treating drug abuse and dependence is best shown in opioids dependent patients experiencing withdrawal [14, 15]. Over the past 40 years, acupuncture and EA have been applied with great success to attenuate behavioral signs of opioid withdrawal in addicts [16-18]. Using acupuncture to treat drug withdrawal symptoms began in 1972. H. L. Wen, a neurosurgeon from Hong Kong, visited China to learn

acupuncture anesthesia. Upon returning to his Hong Kong practice, he used electrical stimulation via acupuncture needles to reduce or eliminate the need for anesthetic drugs during surgery. Acupuncture treatment was given over several weeks prior to surgery, as well as during operational procedures. Dr. Wen was unaware that some patients were also heroin, opium, morphine, alcohol, and/or nicotine dependent. The addict patients later volunteered this information, and reported that they also lost their drug cravings after receiving acupuncture. Wen and his colleagues followed up 40 patients for opium and heroin addiction. They confirmed that 39 of 40 patients were considered improved in that they had gained basal weight and reported they did not crave drugs [19-21].

In the United States, Smith and coworkers [22-25] modified Wen's original protocol by eliminating electrical stimulation and by using an abbreviated prescription of five point auricular acupuncture. This prescription was not designed for withdrawal from any class of drug or any single abused substance. Instead, it effectively reduced cravings, anxiety, and dysphoria of withdrawal in addict patients during withdrawal from a variety of drugs and alcohol. Patients consistently reported the dramatic relief during the early weeks of withdrawal, when the incidence of relapse is highest. By 1974, Smith had used this five-point auricular protocol as the sole detoxification method used in the outpatient clinic at Lincoln Hospital in the Bronx, NY. Over the past 40 years, this acupuncture protocol has grown in popularity. It is currently used to treat alcohol and other drug withdrawal in more than 800 substance abuse treatment centers across the United States and Europe.

Clinical studies and related research on acupuncture have been undertaken by independent groups. Some randomized trials have been done to compare the effects of auricular acupuncture at specific points for the treatment of substance abuse and at sham points [26-28]. Washburn et al. [29] conducted the first controlled study of acupuncture heroin detoxification. One hundred addicted persons were randomly assigned, in a single-blind design, to the standard auricular acupuncture treatment used for addiction or to a "sham" treatment that used points that were geographically close to the standard points. They observed that subjects assigned to the standard treatment attended the acupuncture clinic more days and stayed in treatment longer than those assigned to the sham condition.

Zhang et al. [26] also found that acupuncture and electrical stimulation were more effective than clonidine in treating withdrawal syndromes such as insomnia, pain, and anxiety following acute withdrawal symptoms. Clinical studies have also demonstrated that this treatment has fewer side effects.

In addition, Meade et al. [30] tested the effectiveness of transcutaneous electric acupoint stimulation (TEAS) as an adjunctive treatment for inpatients receiving opioid detoxification with buprenorphine- naloxone at a private psychiatric hospital. It is shown that TEAS is an acceptable, inexpensive adjunctive treatment that is feasible to implement on an inpatient unit and may be a beneficial adjunct to pharmacological treatments for opioid detoxification.

Acupuncture also appears to be a useful adjunct to methadone maintenance therapy (MMT) in heroin addiction. Recently, one study examined the effectiveness of acupuncture for heroin addicts on methadone maintenance by measuring the daily consumption of methadone, variations in the 36-item Short Form Health Survey-36 (SF-36) and Pittsburgh Sleep Quality Index (PSQI) scores. It is shown that acupuncture was also associated with a greater improvement in sleep latency at follow-up. All adverse events were mild in severity [31].

A number of studies have examined the effects of acupuncture on cocaine and alcohol dependence. For example, severe recidivist alcoholic patients treated with acupuncture specifically for the treatment of substance abuse reported less craving for alcohol, fewer drinking episodes, and required fewer admissions to the county detoxification center than did control patients who received acupuncture at nonspecific points [27]. Lipton et al. [32] also reported that patients receiving acupuncture treatment had significantly lower levels of cocaine metabolites than the control subjects. Recently, researchers, headed by S. Kelly Avants, from the division of substance abuse in the Department of Psychiatry at Yale University, divided 82 cocaine addicts into three groups. One third received acupuncture at four specific points around the outer ear, another third received “sham” acupuncture at sites on the ear that would be ineffective, and the remaining third received relaxation therapy consisting of viewing a relaxing video. Treatment sessions were five times a week and lasted eight weeks. The subjects’ urine was tested three times a week for traces of cocaine. They found that patients assigned to receive true acupuncture had less cocaine use compared to the two other groups, and there were a higher percentage of patients in the acupuncture group who were clean from cocaine use by the last week of the study than in the two other groups [6].

The effects of acupuncture on drug addiction have also been verified by animal experiments. It has been well shown that acupuncture suppressed morphine withdrawal syndrome and alcohol-drinking behaviors in rats [33-35]. Furthermore, morphine-induced conditioned place preference can be successfully suppressed by 2 or 100 Hz electroacupuncture, a substitute for classic acupuncture [36, 37].

A recent study by Chae et al. [38] found that acupuncture at ST36, but not the other acupuncture points, significantly attenuated the expected increase in nicotine induced locomotor sensitization to subsequent nicotine challenge. Behavioral response to nicotine challenge in the repeated nicotine treated group (control) was significantly more intense. Stimulation of acupuncture at ST36 just before nicotine challenge as well as during 3 days of withdrawal period completely blocked the effects of nicotine on locomotor activity during the 60 min testing period. In our laboratory, we also found that acupuncture applied at the BL.23 acupuncture point, a novel acupuncture point, could effectively suppress withdrawal syndrome [39,40].

However, some large clinical trials have questioned the effectiveness of acupuncture for drug dependence. In these studies, the acupuncture treatment groups failed to show significant differences from the control group in the treatment of drug dependence [41]. One study has found that acupuncture offered no significant reduction of nicotine withdrawal symptoms or long-term improvement over placebo [42]. Bullock et al. performed a single-blind, randomized, placebo-controlled study to evaluate auricular acupuncture in the treatment of cocaine addiction. Their study had 236 residential and 202 day treatment clients. They did not find any significant treatment differences between true and sham acupuncture. They also found no differences among the three dose levels of true acupuncture [43].

The Cocaine Alternative Treatment Study (CATS) [44] was a large-scale, multi-site study. In this study, 620 patients addicted to cocaine were enrolled from six treatment sites; 412 of the patients were “primary” cocaine-dependent, and 208 were opiate-dependent and maintained on methadone. Patients were randomized to the three treatment conditions:

auricular acupuncture, a needle-insertion control condition, and a relaxation control condition. Treatments were offered five times weekly for 8 weeks. The patients maintained on methadone received standard care as offered in their methadone program. Concurrent drug counseling was also offered to patients in all conditions. The primary outcome measure was cocaine use during treatment and at the 3- and 6-month post randomization follow-up based on urine toxicology screens and retention in treatment. Results of urine samples showed a significant overall reduction in cocaine use, but no differences by treatment condition. There were also no differences between the conditions in treatment retention (44%–46% for the full 8 weeks). In the last week of treatment, 24, 31, and 29% of patients in auricular acupuncture, needle-insertion control, and relaxation control conditions, respectively, were abstinent from cocaine. This large study does not support the use of acupuncture as a stand-alone treatment for cocaine addiction.

4. Effects of acupuncture on psychological symptoms associated with drug addiction

Easing psychological symptoms associated with heroin use and heroin relapse is an important goal in the treatment of heroin dependence. Notably, as the course of withdrawal followed its natural history and acute symptoms abated, acupuncture continued to reduce anxiety and cravings associated with protracted withdrawal. In fact, patients who had completed addiction programs often continued to enjoy stress reduction induced by occasional “booster” acupuncture treatments. There are many ancient and contemporary papers reporting the successful use of acupuncture for the treatment of patients with depression and anxiety disorders [45-50]. Given that the prevalence of depression and anxiety is very high in cocaine and other drug addicts, and depression and anxiety after prolonged abstinence become the main factors contributing to drug relapse and craving, it is very meaningful to pay close attention to the effects of acupuncture on depression treatment among addicts.

In addition, acupuncture has been used to improve psychological status and lessen fatigue [51]. Chang et al. conducted a three-arm randomized controlled trial (RCT) on residents of a homeless veteran rehabilitation program. Sixty-seven enrolled participants were randomly assigned to acupuncture, the relaxation response, or usual care. They found that craving and anxiety levels decreased significantly following one session of acupuncture [52].

In another small, randomized controlled trial, Allen et al. [53] compared symptoms of depression in an acupuncture group, placebo group, and a waitlist control group. The acupuncture group showed greater improvements in depressive scores than the placebo group and the waitlist control group. Roschke et al. [54] studied the effects of adding acupuncture to antidepressant treatment and found that the acupuncture in combination with antidepressant treatment improved the alleviation of depression course compared with pharmaceutical treatment alone.

In a clinical trial using TAES for the suppression of opiate craving in humans, a total of 117 heroin addicts who had completed the process of detoxification for more than 1 month were recruited [55]. They were randomly and evenly assigned into four groups. Three groups received TAES treatment of different frequencies (2, 100, or 2/100 Hz). Self-sticking skin electrodes were placed on four acupoints: Hegu and Laogong (palmar side of the Hegu point) in the left (or right) hand to complete a circuit, and Neiguan and Weiguan in the opposite arm to complete a circuit. The control group was processed as in the previous groups except

that the intensity was minimal (15 Hz, threshold stimulation for 3 min, and then switched to 1 mA thereafter) to serve as a mock TAES control. Visual analog scale (VAS) was used to assess the degree of craving.

There was a very slow decline of the VAS in the mock TAES control group in a period of 1 month. A dramatic decline of the degree of craving was observed in the groups receiving 2 and 2/100 Hz electric stimulation, but not in the group receiving 100 Hz stimulation. These results observed in humans were in line with the findings obtained in the rat: low-frequency TAES is more effective than high-frequency TAES in suppressing the morphine-induced CPP [56].

However, some studies [6, 30, 57, 58] did not show favorable effects of acupuncture on psychological symptoms associated with opioid addiction (anxiety, depression, and craving). For example, Black et al. [59] conducted a randomized controlled study to test the effect of auricular acupuncture in the treatment of anxiety associated with withdrawal from psychoactive drugs. They found that auricular acupuncture was not more effective than sham or treatment setting control in reducing anxiety. We reviewed the clinical studies that have investigated the clinical effectiveness of acupuncture and focused on psychological symptoms associated with opioid addiction. The clinical studies published in Chinese language journals were assessed carefully and included in our systematical reviews. We found that eight studies [26, 29, 41, 44, 60-62,64] included heroin/opioid craving. Seven studies [27, 28, 32, 60-63] included anxiety. Two studies included depression [60, 65]. All of the four studies [44, 66-68] published in English language journals did not show favorable effects of acupuncture on psychological symptoms associated with opioid addiction (anxiety, depression, and craving). Many studies published in Chinese language journals supported the use of acupuncture for controlling psychological symptoms associated with opioid addiction: craving [26, 41, 63, 69,], anxiety [29, 32, 60, 62, 63, 70], and depression [60, 68].

Treatment retention and abstinence are more important goals for the treatment of drug dependence. Effectiveness of the treatment of psychological symptoms associated with drug addiction should be assessed by including longer-term follow-up data. In fact, to determine whether initial improvements from the treatment persist for a reasonable period of time, participant observation should last for at least 3 months. However, most of the studies we reviewed did not provide follow-up data. In these studies, the duration of acupuncture interventions was also shorter than 1 month. In fact, it is unclear whether the extent to which acupuncture has therapeutic effects depends on the duration and frequency of acupuncture. Arguably, longer treatment periods are required for acupuncture to have any chance of showing clinical effects. These variable factors should be taken into account when assessing the effects of acupuncture. Future studies should therefore have sufficiently large samples, extended treatment, and follow-up periods.

5. Possible mechanisms for the effectiveness of acupuncture on drug addiction

It would be reasonable to suggest that an opioidergic mechanism is, at least partially, involved in mediating acupuncture antiwithdrawal. Han and his colleagues from Peking University China have made a detailed survey on the analgesic effect of EA. They found that analgesia induced by 100-Hz EA resulted from accelerating the release of dynorphin from the spinal cord of the rats [11, 71, 72]. In accord with this was the finding that the analgesic effect of 100- Hz EA observed in morphine-dependent rats could be blocked by a high dose of naloxone 202 only [73]. On the other hand, dynorphin has been shown to be the

endogenous ligand of the μ -opioid receptor. Indeed, the withdrawal syndrome observed in rats dependent on morphine can be suppressed by high-frequency electroacupuncture, which accelerates the release of dynorphin in the spinal cord and brain [33, 70, 74]. Morphine-induced conditioned-place preference, an experimental model simulating the craving of heroin addicts, can be effectively suppressed by low-frequency electroacupuncture. This effect can be blocked by a small dose of naloxone, indicating the involvement of endogenous opioid peptides [36, 69].

Meanwhile, the clinical study by V. Clement-Jones et al. also showed that EA was associated with a rise in cerebrospinal fluid met-enkephalin levels in all addicts studied [67]. Recently, Wang et al. [75] found that a downregulation of preprodynorphin (PPD) mRNA level was observed in spinal cord, PAG, and hypothalamus 60 hours after the last morphine injection, which could be reversed by multiple sessions, but not a single session of EA. Accompanied with the decrease of PPD mRNA level, there was an upregulation of p-CREB in the three CNS regions, which was abolished by 100 Hz EA treatment. These findings suggest that downregulation of p-CREB and acceleration of dynorphin synthesis in spinal cord, PAG, and hypothalamus may be implicated in the cumulative effect of multiple 100Hz EA treatment for opioid detoxification.

The mesolimbic dopamine system originates in the ventral tegmental area (VTA) and projects to regions that include the nucleus accumbens and prefrontal cortex, which are believed to play a pivotal role in the development of opiate addiction [20]. Opiate abuse-induced changes in the levels of dopamine in the brain are associated with feelings of well-being and pleasure, providing positive reinforcement of continued opiate abuse [76, 39]. Conversely, withdrawal from chronic opiate administration reduces dopamine outflow in the nucleus accumbens [40, 77]. Furthermore, in the treatment of drug craving and relapse to drug use, the core symptoms of addiction, a non-endorphin-mediated mechanism is probably involved. Lu et al. [78] examined alterations in the firing rate of dopaminergic neurons by means of extracellular recording following chronic morphine exposure and applied 100 Hz electroacupuncture treatment to reverse the reduced firing rate of these neurons. They found that the electrophysiological response of VTA DA neurons to morphine was markedly reduced in chronic morphine-treated rats compared to saline-treated controls. A substantial recovery of the reactivity of VTA DA neurons to morphine was observed in rats that received 100 Hz EA for 10 days.

Evidence also indicates that acupuncture acts on the nucleus accumbens to inhibit the elevation in dopamine [79, 80]. Yoon et al. demonstrated the acupuncture-mediated inhibition of ethanol-induced dopamine released in the rat nucleus accumbens through the GABAB receptor [80]. Chae et al. showed that acupuncture treatment at ST.36 attenuated the expected increase in nicotine-induced locomotor activity by reducing postsynaptic neuronal activity in the nucleus and striatum [38].

Δ FosB and FosB are members of the Fos family of transcription factors implicated in neural plasticity in drug addiction. Li et al. [81] found that the intake of and preference for ethanol in rats under 100 Hz, but not 2 Hz electroacupuncture, regimen were sharply reduced. The reduction was maintained for at least 72 hours after the termination of electroacupuncture treatment. Conversely, 100 Hz electroacupuncture did not alter the intake of and preference for the natural rewarding agent sucrose. Additionally, FosB/ Δ FosB levels in the prefrontal cortex, striatal region, and the posterior region of ventral tegmental area were increased

Role of Acupuncture in the Treatment of Drug Addiction <http://dx.doi.org/10.5772/60655> 203 following excessive ethanol consumption, but were reduced after 6-day 100 Hz electroacupuncture. Interestingly, EA can inhibit CB1 receptor upregulation in the prefrontal cortex, striatum, hippocampus, amygdala, and ventral tegmental area in ethanol-withdrawn mice [82]. Furthermore, extracellular signal-regulated kinase (ERK) plays a role in neuronal changes induced by repeated drug exposure. EA can reverse ethanol-induced locomotor sensitization and subsequent ERK expression in mice [83]. These results suggest that acupuncture could play an important role in suppressing the potentiating effects of ethanol and other drugs.

Our recent study [41] showed that acupuncture attenuated elevated c-fos expression in the central nucleus of the amygdala (CeA) during morphine withdrawal in rats. Some studies emphasize that the motivational components of opiate withdrawal appear to be centrally mediated by limbic structures such as the nucleus accumbens and amygdala [2-4]. Therefore, elevated c-fos expression in the CeA might be associated with the motivational components of opiate withdrawal. Our observation that acupuncture suppressed elevated c-fos expression in the CeA indicated that acupuncture might have some therapeutic effects in the treatment of the negative motivations of opiate withdrawal. Of course, further studies must be performed to clarify this issue.

In addition, the CeA and the basolateral amygdala have been extensively and differentially involved in associative learning and memory processes, attributing affective salience to environmental stimuli paired with drug effects [5]. One theory of the neural mechanisms of drug abuse focuses on various learning and memory systems in which the normal functions of these complex neural circuits become subverted leading to compulsive drug-seeking behaviors [84, 85]. In this model, drugs of abuse initiate plasticity mechanisms in different learning and memory systems that come to control behaviors of the individual over other preexisting memories. Experience with addictive drugs are encoded and stored like other experiences, except that drugs of abuse only mimic a subset of the actions of natural reinforcers in the brain.

Acupuncture can affect learning and memorizing ability [1, 7, 86, 87]. Further work is needed to emphasize whether acupuncture can re-encode experience with addictive drug via affecting learning and memory systems, and modify the addictive behaviors. The amygdala acquires information that promotes approach and interaction with drug-associated stimuli. We also need to know which role the amygdala plays when acupuncture stimulation affects drug-associated learning and memory.

6. Discussion In terms of lives and productivity, drug addiction remains one of the most serious threats to our public health.

Addiction can be defined as the loss of control over drug use, or the compulsive seeking and taking of a drug regardless of the consequences. Available treatments for addiction remain inadequately effective for most individuals. Incorporating acupuncture into existing therapies offers a promising approach. Acupuncture has been widely recognized as a valuable, readily available, and safe means of health care. It is effective, inexpensive, and requires only simple equipment. In this review, we identify and summarize the evidence about the possible clinical effectiveness of acupuncture on drug addiction, including withdrawal symptoms, drug craving, depression, and anxiety. We also discuss the theory and possible mechanisms for the effectiveness of acupuncture. Some animal and clinical studies have

provided supporting evidence for the promising effects of acupuncture. Unfortunately, the data do not allow us to make conclusions that acupuncture was an effective treatment for drug addiction. The evidence for its effectiveness has been inconclusive and difficult to interpret [63]. Some of the clinical studies were unable to detect statistically significant differences in treatment efficacy between their acupuncture treatment and control groups [66-68].

In addition, there are few randomized controlled clinical trials of acupuncture treatment for drug addiction, and the methodological methods used in several clinical trials of acupuncture treatment for drug dependence can be criticized for their poor quality. The quality issues include the following: small numbers of patients, no control subjects, lack of randomized assignment, lack of details regarding specific point locations for needle insertion, and no specification regarding the degree of blinding among research subjects.

In fact, there are some variable factors that need to be taken into account when assessing the effects of acupuncture on drug addiction.

(1) The study protocol may influence the assessment of effectiveness of acupuncture. Methods and research designs have been issues of debate among acupuncture clinicians and researchers [88]. For a methodological perspective, randomized controlled trials are considered the gold standard in terms of identifying differences in treatment efficacy [89]. However, unlike the evaluation of a new drug, randomized controlled trials of acupuncture are extremely difficult to conduct, particularly if they have to be blind in design and acupuncture has to be compared with a placebo [90]. The efficacy of acupuncture is difficult to study empirically because of the fundamental divergence between the two schools of thought. The gold standard in Western science is randomized, double-blind, and controlled trials, utilizing one specific protocol for each condition. Randomized controlled trials can be used to answer questions about most clinical problems. However, this approach is not always a practical and cost-effective solution. Sometimes randomized controlled trials are open to error; for instance, patient preference may have an effect on the results as may certain cultural environments. In addition, in some Asian countries such as China where acupuncture is widely used, most patients know a great deal about acupuncture, including the special sensation that should be felt after insertion or during manipulation of the needle. Although various “sham” or “placebo” acupuncture procedures have been designed, they are not easy to perform in these countries. Moreover, acupuncturists consider these procedures unethical because they are already convinced that acupuncture is effective. In fact, most of the placebo-controlled clinical trials have been undertaken in countries where there is skepticism about acupuncture, as well as considerable interest.

(2) Another difficulty in evaluating acupuncture practice is that the therapeutic effect depends greatly on the proficiency of the acupuncturists. Their ability and skill in selecting and locating the acupuncture points and in manipulating the needles are different. Needling techniques of inserting, retaining, stimulating, and withdrawing are difficult to standardize. This may partly explain the disparities or inconsistencies in the results reported by different authors, even when their studies were carried out on equally sound methodological bases.

(3) In traditional Chinese medical system, such as acupuncture, where each individual is treated according to specific conditions and symptoms, it may be invalid to use the same protocol for every condition. Individualized protocols are critical to the success of the acupuncture treatment. For example, acupuncture stimulation typically elicits a composite of

sensations termed deqi, manifesting as soreness, numbness, heaviness, and distention [91]. A body of clinical and experimental evidence indicates that the presence of the deqi sensation is a prerequisite for, and often an indicator of, a clinical acupuncture effect. Traditionally, patients are asked to remain aware of the sensation during acupuncture treatment. Deqi may be an important variable in studies of the efficacy and mechanism of the action of acupuncture treatment. Our previous study showed that the deqi sensations of heroin addicts were significantly higher than those of healthy subjects during acupuncture stimulation, indicating that heroin addicts are “good” responders to acupuncture stimulation [92].

(4) Acupuncture was developed as a branch of traditional Chinese medicine on the basis of oriental philosophy, which takes a holistic approach to regulating the balance of the human body. (Several different schools of acupuncture exist, each with its own principles.) These principles may vary with the types of acupuncture being investigated. The inconsistency in treatment protocols between studies, or the use of combined therapies, makes it impossible to draw a strong causal relationship between therapy and its treatment effect, thus making replication of studies difficult. To this end, traditional knowledge and experience of acupuncture should be duly represented by the investigation team when research is proposed, prepared, and conducted. A good clinical study on acupuncture may be conducted with the understanding and integration of both traditional and modern knowledge of medicine;

(5) Most of the clinical research on acupuncture in the United States focused on auricular acupuncture, which is simply the insertion of acupuncture needles into prespecified locations in the ear, whereas studies from China used body acupuncture to treat opiate addiction. These findings are intriguing considering that acupuncture on body and auricular points exhibited different efficacies. According to our clinical experience and the theory of traditional Chinese medicine, body acupuncture may need more attention. Some acupuncture points represent discrete locations in the body, where manual or electrical stimulation can exhibit therapeutic effects on cocaine and other drug addiction [26, 28, 60, 61, 93]. Table 1 **[See Below]** provides the summary of main acupoints/sites selected in the reviewed studies.

In China, body acupuncture, rather than ear acupuncture, was commonly used for the treatment of drug addiction [26, 28, 60]. The acupuncture points most frequently selected are Zusanli (ST.36), Sanyinjiao (SP.6), Neiguan (PC.6), Shenmen (HT.7), Laogong (PC.8), Waiguan (TE.5), and Hegu (LI.15), located on the four limbs. In our recent work, we showed for the first time that acupuncture applied at the BL.23 acupuncture point, located on the back and commonly used for analgesia and sedation in our clinic, could effectively suppress withdrawal syndrome [40, 41]. Clinically, BL.23 could provide us with a new selection of effective acupuncture points for successful treatment of drug addiction. Further studies on the synergistic combination of BL. 23 and other effective acupuncture points, such as Zusanli (ST.36) and Sanyinjiao (SP.6), could assist acupuncturists to use a balanced and appropriate choice for combining points in the treatment of addicts.

Acupoints appearing in the literature

Table 1. Summary of main acupoints/sites selected in the reviewed studies

<u>Acupoints</u>	<u>FX of appearance (N)</u>	<u>%</u>	<u>Acupoints appearing in the literature</u>
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Neiguan (PC6)	12	11.11	6,26, 27, 28, 29, 41,44, 62, 63, 64,65 and 68
Zusanli (ST36)	10	9.26	6,26, 63, 29, 68, 28, 27, 41, 44, and 62
Sanyinjiao (SP6)	8	7.41	6,26, 27,28,44,62,63,and 68
Shenmen (HT7)	7	6.48	26, 28, 41, 62,63,65, and 68
Hegu (LI4)	6	5.56	6, 26, 27,44, 64, and 68
Shenmen (ear)	4	3.70	3,5, 60, and 68
Kidney (ear)	4	3.70	3,5, 60, and 68
Liver (ear)	4	3.70	3,5, 60, and 68
Lung (ear)	4	3.70	3,5, 60, and 68
Sympathetic (ear)	4	3.70	3,5, 60, and 68
Laogong (PC8)	4	3.70	6,44,65, and 68
Sishencong (EX 6, 27, and 65	HN1)	3	2.78
Jiaji (EX 28, 62, and 63	B2)	3	1.85
Shenshu	3	1.85	28, 62, and 63
Taichong	2	1.85	29 and 63
Baihui (GV20)	2	1.85	41 and 61
Waiguan (SJ5)	2	1.85	26 and 44
Zhiyang (GV9)	2	1.85	29 and 61
Fengchi	1	0.93	29
Anmian	1	0.93	29
Dazhui (GV14)	1	0.93	61
Mingmen (GV4)	1	1.85	61

Shendao (GV11)	1	0.93	61
Lingtai (GV10)	1	0.93	61
Shenting	1	0.93	65
Naokong	1	0.93	65
Yintang	1	0.93	65
Yangbai	1	0.93	65
Yongquan	1	0.93	65
Quanzhong	1	0.93	65
Naohu	1	0.93	65
Ben Shen	1	0.93	65

In summary, acupuncture offer some advantages over existing pharmacological interventions: they are safer, have fewer side effects, and are less expensive. Since deteriorating health often accompanies long-term use of addictive drugs, pharmaceutical interventions with harsh side effects can be detrimental to the general health of long-term drug users. In contrast, acupuncture can enhance immune function and increase metabolism in organs necessary to fight infections and various acute and chronic illnesses. Although the definitive role of acupuncture in the treatment of drug addiction has yet to be established, its basic research and clinical data reviewed here justify further clinical trials to systematically examine the efficacy of acupuncture in treating various conditions related to drug addiction such as withdrawal symptoms, drug craving, anxiety, and depression. The next important step in acupuncture research is to get a better understanding of the neurochemical mechanism of acupuncture in order that the therapeutic effects of acupuncture can be further improved. Also scientifically conducted clinical research is needed to examine the effectiveness of acupuncture treatment of drug addicts. As we mentioned in this review, it has proved difficult to apply and integrate the basic principles and methodology of modern science that ensure the reliability of research subjects to clinical studies on acupuncture. However, researchers should be encouraged to ensure the highest possible standards of study design and reporting in future research in order to improve the evidence base in this field.

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A. The Protocols Developed by Dr. Donald (Deke) Kendall

Dr. Kendall has been a pioneer in the field of acupuncture and TCM herbal research for forty years and was one of the founders of the National Guild for Acupuncture and Oriental Medicine, OPEIU #62, AFL-CIO. He is author of **Dao of Chinese Medicine** published by Oxford University Press, one of the most respected books in the field.

"All in all, the contribution of this book to the study of medicine is great."

--Focus on Alternative and Complementary Therapies

In the following monograph, excerpted just to cover the treatment of opioid addictions, Dr. Kendall explains the underlying physiological impact of acupuncture on the neurotransmitters that are involved with the brain chemistry of addiction. He wisely discerns that treatment is most effective when using 2 Hz continuous electro-acupuncture (EA) stimulation on the needles. This judgment is supported by the reams of research which follow in **B. Additional Studies on the Efficacy of Acupuncture for Withdrawal from Opioids**.

My advice to the reader is simply to follow Dr. Kendall's protocol and avoid the acupuncture treatment strategies other than his which have been previously discussed in **A. Additional Studies on the Efficacy of Acupuncture for Withdrawal from Opioids**.

I personally have tried most if not all of them, and by far the most effective and simplest is the protocol developed by Dr. Kendall. If you appreciate good science, you'll enjoy it.

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Treatment of Substance Addiction With Acupuncture

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Abstract: Acupuncture been applied to treat drug addiction since 1972 when H.L. Wen (Wen and Hueng, 1975) first observed that electroacupuncture could relieve the symptoms of heroin withdrawal. This initiated several investigations into using acupuncture to alleviate the symptoms of abstinence syndrome brought on by acute withdrawal of drugs. Only moderate success was obtained from some of these initial explorations and treatment approaches were not consistent from study to study. These early efforts were carefully analyzed to determine what factors including point selection, duration of treatment number and spacing of treatments, stimulation frequency (Hz.), etc., that resulted in a more reliable outcome. Based on this information and considering the characteristics of the metabolic detoxification of each particular substance, protocols were devised that resulted in a rational and consistent clinical approach in treating drug addiction. These are described below for several different drugs and nicotine.

More than 2000 individuals were treated from 1981 through 1985, for a variety of substances which mostly involved nicotine (smoking) but also included marijuana, cocaine, alcohol, heroine, methadone and other opiates. An extremely high initial success rate (95-98%), which was taken as complete detoxification without any use of the substance, was achieved for all drugs. Follow up after

one year showed excellent results (65-80%) for all substances. The recidivism was higher for heroin and methadone users that had been successfully detoxified and it seems that it was very difficult for some of them to break away from their previous life styles and sociological situations. They also seemed not to handle subsequent stress episodes well. This clinical effort was not originally designed as a controlled study since the most important goal was to develop repeatable and consistent treatment protocols.

The detoxification success rate of the above effort is considered accurate, even though not verified by urine or other tests. Recidivism data, however, was not rigorous. Determination of accurate recidivism was difficult because the clinic trials were not set up to efficiently obtain follow up information. Not all persons that were treated could be located and some showed a slight resentment about being checked on even though they were still drug or nicotine free. There is need for more and better controlled studies that are designed to account for the problem of obtaining accurate follow up information.

Post treatment support is extremely important and where individuals could be given or taught successful coping strategies to deal with future stress exposure or physical memory related to drug use, especially in smokers, they did better. Some patients were taught active and passive relaxation techniques and all were advised to immediately seek treatment if uncontrollable urges or events were causing them to again consider smoking or drug use. They were also advised that if they inadvertently smoked or used drugs or if they were coerced or badgered into using drugs or tobacco again, to immediately come in for treatment to avoid setting up long term addiction. Those that came in for occasional unscheduled follow up or support usually only required one treatment to get through the problem period. Some patients scheduled regular follow up or maintenance treatments every six months just to make sure they did not get any urges to relapse into drug or

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nicotine use. This is one of the truly important and unique features of acupuncture therapy in that it can be easily and immediately applied in almost any circumstance. The other important feature in using acupuncture to treat addictions is that many people have tried every program available in an attempt to get off drugs, alcohol or to stop smoking without any success. Since acupuncture therapy is mainly directed toward restoring disrupted neurochemical balance brought on by addiction and subsequent abstinence, it has been very effective.

The treatment philosophy described below represents one particular approach and it is geared to outpatient consideration although the procedures work just as effective on an inpatient basis. Treatment protocols were developed to obtain the most successful, predictable and consistent results. Mild electroacupuncture stimulation is applied to some of the acupoints and this requires that the practitioner be properly trained in its use as well as in use of acupuncture itself. A trained professional acupuncturist should always be employed whenever acupuncture therapy is applied for the treatment of any condition. Less formal procedures have been applied by some groups that do not utilize electroacupuncture and they also report good results, however, statistical and follow up data was not provided in the early studies (Smith, 1979; Shakur and Smith, 1979; Smith et al, 1982, 1984) although more recent information involving crack cocaine is showing great promise (Smith, 1988).

It is generally recognized that outpatient treatment for the hard drugs has a much lower chance for success since the subject can have ready access to drugs. This is complicated by the fact that the drug supplier may not want to lose a client and therefore encourages the user to take the easy way out to avoid withdrawal and return to drugs or at least try it one more time. The other problem is the ever present peer pressure. A mistaken thought is that peer pressure is operative only in the young and impressionable; however, it appears that it is a strong factor in adults of all ages as well. Many failures to stay off even cigarettes can be directly traced to an active smoking family member or friend that encourages the person to smoke again because they are possibly threatened by the fact that the other person is trying to get off nicotine. The seriousness of this problem was illustrated by Man and Chuang (1980) who observed, in a methadone detoxification study involving 35 patients over a 6 month follow-up period, that there was an 82.9 % incidence of illegal drug use as verified by urine tests.

Despite the availability of drugs, nicotine and alcohol, many people have been successful in getting off these substances with acupuncture on an outpatient basis. If people voluntarily want to abstain from an addictive substance the chances for success are probably higher than for those subjects that are coerced or forced to withdraw due to family or legal pressure. Strong individual motivation undoubtedly contributes to the long term success after the initial detoxification although acupuncture has been successful in subjects that were unsure of their desire to quit using a particular substance. Health status or physical situation, such as being pregnant, can also provide inspiration to abstain from a drug after getting through the initial detoxification. Elderly patients that had been hospitalized with serious illnesses involving the lung and heart, for example, had a very high rate of success in nicotine withdrawal (Zaleskly, et al, 1983).

Background

There is little question that drug and substance abuse is perhaps the single most significant health hazard facing the world population today. Nicotine use alone in the United States may be directly related to at least 600,000 premature deaths each year. Although much attention is now being focused on this serious problem, drug abuse has been a major concern to the medical establishment for more than 100 years (Cownt, 1986a). Fortunately, early recognition of the potential for widespread addiction of the public to opiates and other drugs was influential in restricting their use in prescription and patent medicine (Simmons, 1906). It is estimated that before the FDA regulations to ban the use of opiates that perhaps one in every 400 Americans were already addicted to their use (Musto, 1973). Narcotic laws to enforce the ban were effective and by the 1930s there was a ten fold

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The latest concern is the uncontrolled illegal importation and widespread use of cocaine. The addictive nature and hazards of cocaine use were also recognized long ago and FDA regulations have restricted its use in medicines as well. On the other hand, the public is apparently not aware of its risk because the illegal use of cocaine is pandemic. It is difficult to estimate how widespread it is being used but numbers range from 5.4 million Americans had tried it at least once by 1974 to 21.6 million in 1982 to approximately 25 million by 1986 (NIDA, 85:1414, 1985). It is estimated that there were 4 to 5 million regular users by 1985 (Amer. Fam. Phys. 31:173-176, 1985).

Substance abuse over the history of civilized man has been a complex problem because it is driven by strong economic factors that have even involved entire governments of some countries in the production and sale, usually to another country, of addictive products. It has led to wars between countries or wars to enforce the illegal import of the substance, such as the opium wars fought against China. Many of the armed conflicts in the world today are related to controlling the drug traffic in various parts of the world. The economic leverage of cocaine alone has also resulted in widespread corruption in many countries to subvert the legal systems designed to detect and enforce the laws against its distribution and use. The situation of cocaine today in the United States is reminiscent of the situation that existed 140 years ago in China. The British raised opium in India and illegally imported it into China and eventually enslaved an entire country for more than 100 years.

Many people have the idea that the solution to the problem is very simple, all one has to do is to tell the users to stop buying the drugs. However there are complications in this simple approach. First, once an individual is addicted to a substance they have little desire to stop its use and in fact many will do almost anything or go to any limits to obtain the drug involved. Even when they are successfully treated for the addiction of a substance they consciously return to its use for a variety of very weak reasons.

The power of drug dependence has been demonstrated in rats and monkeys that will press a lever to obtain intravenous alcohol, amphetamines, opiates or cocaine in deference to eating or drinking water. It has been demonstrated that monkeys prefer to press a lever to obtain intravenous cocaine instead of intravenous amphetamines, or food, although they may be starving or to having sex with a receptive female. If given a choice between a lever that dispenses a high dose of cocaine accompanied by a strong electric shock or a low dose with no shock they prefer the former. Monkeys will continue these behaviors until they die of convulsions or exhaustion (Bull. Narc. 36:3-14, 1986).

These forces have a continuing strong influence on individuals even though they have successfully gone through detoxification leading to eventual return to drug or nicotine use. Previously it has been estimated that the recidivism rate may be as high as 75% for all types of substances which is reached in one or two years after stopping drug use. This points out the need for continuing support and education for persons once they have been detoxed. It also seems that a crucial phase of the recovery occurs approximately six weeks after drug cessation where a strong urge, desire or curiosity to experiment with the drug or nicotine just one more time to demonstrate to the former addict that they have complete control over their problem. This is a very critical period and some refer to it as the six week wall. Patients need to be advised of the increased risk at this time so they know how to cope with the situation if it arises. For alcohol and opiates a follow up treatment should be scheduled at the sixth week.

The success of the stop smoking program conducted for many years in Bad Nauheim, Germany where they report an initial quit rate of 82.4% for 12,000 subjects with a 50.2% success after 10 years illustrates the importance of follow up support (Hammer, 1981). Although acupuncture was used as a treatment modality they approached nicotine addiction mainly as a behavior problem. The follow up included educating the subjects concerning the effect of nicotine on the body, analysis and effect of tobacco advertising, autogenic training to break body memory or conditioning due to smoking, yoga exercises, running, baths, films, slides, etc.

Strong education and awareness programs are vital to alert the public to the risks and

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consequences of substance abuse. The present trend toward reducing the percentage of people using nicotine is directly related to providing the public with information on the risk of smoking. This even includes the risk to non-smoking adults and children exposed to secondary cigarette, cigar and

pipe smoke.

With the deaths in 1986 of two nationally known professional athletes in separate incidents, where cocaine was apparently used for the first time, the public is just starting to realize the risks associated with this dangerous drug (Cowart, 1986b.). Increased incidence of stroke and fatal heart attacks in younger people is also being observed because of cocaine's influence on raising blood pressure and damaging effects on the heart (Amer. J. Card. 57:496, 1986a; 57:1185-1186, 1986b; Arch. Pathol. Lab. Med. 110:479-484, 1986).

Another complication in treating drug dependence is that until now there has not been any effective and humane approach to help treat the withdrawal syndrome without the use of additional drugs. The proper application of modern acupuncture may be one of the few modalities that have promise of providing a potentially successful program in treating those individuals attempting to abstain from the use of drugs.

Philosophical Considerations

The main view point in traditional Chinese medicine (TCM) in regard to substance abuse and addiction is that it is essentially a physiological problem which then can have psychological consequences. This is borne out by the knowledge that almost all smokers (nicotine addicts) started using tobacco when they were children experimenting with the forbidden fruits of adults. They really did not have any underlying psychological problems that drove them to nicotine. The same applies to alcohol as well since almost all drinkers got their start when they were young teenagers. One recent finding, however, showed that 50% of young alcoholics came from families with two alcoholic parents and another 25% had one alcoholic parent. This possibly indicates the importance of family influence on the behavior on their children.

It has been noted by Gawin and Kleber (1985) that although the presence of affective behavior problems may increase an individual's potential for drug use, 50 to 70% of abusers do not have psychiatric diagnoses. Peer pressure and the promise of euphoric bliss or group acceptance are probably the most important factors to induce individuals to try drugs for the first time. Most who tried were not aware of the addictive powers of the substance involved and physiological habituation occurred before they knew what was happening. If the substance is withheld after this point then abstinence or withdrawal syndrome becomes apparent. The subject then has to continue using the substance just to avoid the misery of withdrawal symptoms. It is also possible that some people continue the use of drugs just to once again achieve that first euphoric high only to find out that it can not be re-experienced. This is because the most significant influence on central neurotransmitter production that produces the "high" occurs during the initial habituation phase. Once dependence is achieved the affected neurons are inhibited and additional drug intake only maintains the habituation and the state of tolerance is established.

One of the major differences in treating addictions by a primarily physiological approach, such as acupuncture, is dealing with the nomenclature or classification of the disorder. Labels such as "incurable disease" have been popularized, especially associated with alcoholism, presumably to allow the public to get the idea that it is only a case of happenstance or perhaps genetics that one individual is or is not afflicted. This classification scenario developed on the thought that if one has an incurable disease then it is okay to have it treated. The downside problem with this approach is that an individual's self esteem is damaged by being stuck with the label of "incurable" or worse yet "bad genes".

Some experts point out that substance abuse must be an incurable disease since whenever a former user of some substance tries it again they are immediately re-addicted. As it turns out this is also true if anyone including naive subjects uses almost any addictive substance, they will become addicted. Therefore any successful approach requires that the recovered addict abstain from any use of the particular substance in order to remain addiction free.

Since the addicted state causes a wide range of possible aberrant behavior, perhaps dependent somewhat on the particular drug involved, then heavy psycho-sociological counseling has usually been included in the former treatment approaches. Often this has included several weeks of

hospitalization and the use of other drugs to treat the withdrawal syndrome. The experience in using acupuncture indicates that once an individual is successfully detoxified that most of the affective behavior disorders significantly decrease or disappear. Remaining problems may then also be treatable with acupuncture. Some percentage of individuals, especially younger people, may need to be referred to counseling to resolve remaining deep-seated problems.

The treatment of substance abuse with the utilization of acupuncture is based on the fact that all animals, including humans, are addictable to many natural and artificial chemical substances. The addiction or habituation process occurs because of the effect that these substances have on certain brain centers and peripheral tissue. It is entirely independent of any weakness or propensity toward development of addiction. So the concept of disease and especially incurable disease is not involved. It is true that whenever a former addict uses a particular substance again they will more than likely become re-addicted just as they did the first time they were involved with that substance. Re-addiction occurs easier probably because of the physical memory that persists as result of conditioning neuronal circuits during the previous habituated state. This may be one of the underlying factors related to the high rate of recidivism.

Addicted State Where Chronic Drug Or Substance Use Required To Stimulate Deficit In Neurochemicals in Order To Avoid Withdrawal Syndrome.

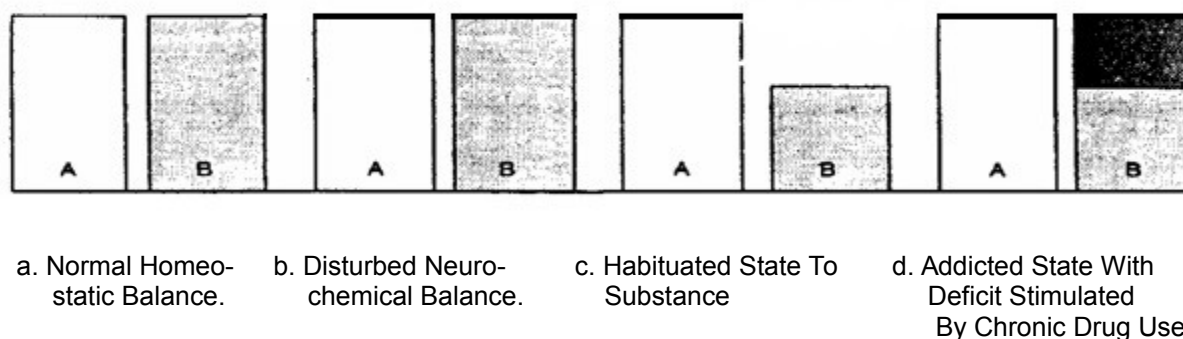


Figure 1. Central Neurochemical Model For Substance Habituation and Addiction Indicating Normal Homeostatic Balance (a.); Disturbed Neurochemical Stimulation Due To Initial Substance Use (b.); Habituation Of Neuronal Centers (c.) And Addicted State That Requires Chronic Use Of Substance To Avoid Withdrawal Syndrome (d.).

Addiction Model

The application of acupuncture to treat drug use is based on a neurochemical receptor hypothesis for drug, nicotine and alcohol addiction (See, Ramsey, 1977; Stinnett, 1977; Snyder, 1980; Gillman and Lichtigfeld, 1983). The particular model as illustrated in Figure 1. considers the central system neurochemical and neuroactive make-up to be broadly classified into two categories. The first (Group A) mediate activities characterized by sympathetic outflow which includes increased heart rate, higher blood pressure, inhibition of the gastrointestinal system, decreased lacrimation and salivation as well as many other functions. These basically are all the responses to stress stimuli. Group B on the other hand are those that predominate during parasympathetic

activity including lowering heart rate and blood pressure, activating the gastrointestinal system, increasing salivation and lacrimation plus other activities. These are opposite to the stress reaction and are typical in relaxation, meditation and sleep. In TCM terms Group A would be classed as Yang and Group B as Yin. Homeostatic balance occurs when these two groups of neurochemicals, yin and yang, are in equilibrium at their normal levels (See Figure 1.a).

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The initial response to drug use in an inexperienced or naive individual is characterized by a marked increase of the Group A (Yang) central transmitters along with a significant elevation of the Group B (Yin) substances (See Figure 1.b). It can produce euphoria, a rush or the so-called initial high. The response can be so extraordinary that nausea, vomiting, dizziness and even unconsciousness can also result. This is very often experienced with the first time use of opiates and alcohol as well as tobacco products. It is also now understood that the induced imbalance due to many drugs, especially opiates and cocaine, is so significant that death can also be a consequence of first time use.

Support for the supposition concerning over stimulation or production of transmitters is provided by the observation that acute administration of opiates depletes CNS levels of norepinephrine (NE) and dopamine (DA). However, this effect can not be induced in tolerant animals. Also, the development of tolerance can be blocked in some animals by inhibiting the synthesis of NE which also can decrease withdrawal or abstinence syndrome.

Apparently cocaine also has a pronounced initial effect on the Group A transmitters mainly involving dopamine which could cause a significant increase in blood pressure and heart rate. This is the suspected mechanism that has resulted in stroke and heart failure in some even first time users. The net effect of these exogenous drugs is to stimulate many areas in the brain including the serotonergic nuclei of the brain stem and perhaps catecholamines involving alpha receptors. The release of catecholamines due to cocaine use could also provoke stress induced analgesia which would account for the report of total freedom of pain during the cocaine high. The other mechanism for producing analgesia could also be that cocaine activates the serotonergic and noradrenergic descending endogenous pain control system that is activated by acupuncture.

Continued use of a substance and subsequent production of central neurochemicals eventually, and often rapidly, causes habituation or tolerance resulting in the inhibition of neuronal pathways and circuits. Some substances, even including nicotine, are so potent that addiction can occur in many people with just a one time use. The habituated state is illustrated by Figure 1.c. which is mainly characterized by inhibition of certain brain nuclei and circuits that utilizes Group B transmitters. The suppression of Group B results in a relatively higher level of Group A which induces an apparent sympathetic outflow which can result in the presentation of abstinent or withdrawal syndrome. So in order to avoid the misery of withdrawal brought on by this central neurochemical imbalance, the individual needs to intake additional drugs to stimulate Group B neurochemicals in an attempt to maintain some simlance of homeostatic balance (See Figure 1.d.). When an addicted individual stops using a particular drug that maintains the induced higher levels of Group B, the condition noted by Figure 1.c will result and the individual will experience withdrawal syndrome. This condition (Figure 1.c.) would be classed in TCM as an apparent Yang excess due to a deficiency of Yin and for this reason addiction is considered to be a Yin deficiency. The application of acupuncture reactivates the inhibited neural centers and then the individual can abstain from the drug use without experiencing withdrawal.

Tolerance and physical dependence (habituation) usually occur together but they are not necessarily identical in nature. Tolerance relates to the characteristics of the drug wherein increasing amounts are required to achieve the same physiological effect. Metabolic tolerance may also be present and it involves increased production of certain enzymes that breakdown the substance, especially in the liver, that increase in response to chronic drug, alcohol and nicotine intake. Physical dependence or habituation is the state of inhibited or depleted neural centers which produce physiological responses

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which are manifested as abstinence syndrome when administration of drug is discontinued or withdrawn.

Tolerance to a substance may develop without habituation, such as occurs with the chronic intake of large doses of a vitamin, which does not produce abstinence syndrome when withdrawn. Likewise habituation may occur with a single dose of a drug, such as methadone, which will produce abstinence syndrome but tolerance is not yet established. For all major drugs, alcohol and nicotine these differences associated with habituation and tolerance cannot be separated.

Mechanisms of Acupuncture in Treating Addictions

The discovery that electroacupuncture could relieve the symptoms of heroin withdrawal (Wen and Cheung, 1975) occurred at about the same time that studies were being performed to comprehend the physiological mechanisms of acupuncture mostly related to analgesia. There are many common pathways between the endogenous pain controlling systems and those which respond to drug, nicotine and alcohol use. Even though some drugs such as amphetamines, cocaine and nicotine are considered stimulants and others are depressants, such as alcohol and opiates, they all have profound influence on the production of catecholamines, serotonin and endogenous opiates. Each addictive substance may primarily affect only one particular central transmitter or neurochemical but most of these have functional interrelationships. Consequently there are general responses in the addictive process involving many common substances.

There is a correlation between the pharmacological agents that stimulate central neurochemicals to produce physical dependence and tolerance and the central processes that are activated by acupuncture. Just as overstimulation of these central nuclei by exogenous substances cause habituation, long duration (several hours) or repeated application of electroacupuncture stimulation can also produce tolerance. This tolerance shows cross tolerance with morphine (Han and Tang, 1981; Zhou, et al, 1985; Han, et al, 1985; Tang, et al, 1985). serotonin (Li, et al, 1982; Li, et al, 1985) and norepinephrine (Xie, et al, 1984; Xie, et al, 1985). Once electroacupuncture tolerance is achieved further stimulation will fail to produce significant analgesia. Acupuncture stimulation, however, does not produce physical dependence. Cheng, Pomeranz and Yu (1980), however, observed that electroacupuncture treatment of morphine dependent mice reduced signs of withdrawal, without showing cross tolerance.

Common pathways are also demonstrated by the fact that certain pharmacological agents can either enhance acupuncture analgesia or cause it to be attenuated (Han, et al, 1980; Han and Terenius, 1982). Many of these same agents can influence abstinence syndrome with an increase of acute symptoms correlating with attenuation of acupuncture analgesia (AA) and a decrease associated with the augmentation of (AA). The opiate antagonist naloxone, for example, can produce immediate presentation of abstinence syndrome in a chronic heroin user. Naloxone also blocks the analgesia produced by acupuncture stimulation (Mayer, 1977; Chapman, 1977; Malizia, 1978). Acupuncture analgesia is also attenuated by an influence on central catecholamines involving alpha receptors. GABA and cAMP (See Table 1, left hand column) and is augmented by serotonin, endogenous opiates, acetylcholine, prostaglandin E and cGMP (See Table 1, right hand column). These would correspond to Group A and B respectively noted in Figure 1. The main central neurochemicals or neurotransmitters involved that are jointly influenced by drug use and acupuncture stimulation are as follows:

Serotonin (5-Hydroxytryptamine, 5HT)

Central serotonin may be most important in the final pathway involved both in the mediation of acupuncture analgesia and the physiological effects of drugs and subsequent development of habituation and tolerance. Acupuncture induced analgesia and acute administration of morphine both cause an increased release of brain 5HT (Yi, et al, 1977). Liang, et al (1981), also observed that the individual variations in acupuncture analgesia in rat was directly related to brain levels of endogenous opiates and serotonin. Tolerance to electroacupuncture is reversed by microinjection of 5HT into the nuclei accumbens in rabbit (Xuan, et al, 1982) and both electroacupuncture and morphine tolerance is reversed by intraventricular or intracerebral injection of 5HT (Xuan, et al, 1985) or the intraventricular injection of the 5HT precursor, 5-hydroxytryptophan (5HTP) in rat (Li, et al, 1982). Intraperitoneal injection of 5HTP also produces tolerance that shows a cross tolerance with electroacupuncture analgesia and morphine (Li, et al, 1985).

Endogenous Opiates

It is quite obvious that the use of exogenous opiates has a profound influence on endogenous opiate receptors. Naloxone, an opiate receptor blocker, can bring on abrupt withdrawal syndrome in heroin addicts and in morphine dependent rats (Lorenz, et al, 1975). It can also block or attenuate the analgesia produced by electrical stimulation or electroacupuncture (Mayer, 1977; Chapman, 1977) in

human subjects and animals as well. Naloxone administered after acupuncture therapy could cancel the beneficial effect of reducing withdrawal symptoms in nicotine, marijuana and alcohol users (Malizia, 1978). However, abstinence syndrome can be repressed in opiate dependent animals (Lorenz, et al, 1975; Wen, et al, 1979) and human subjects (Wen, 1977), given naloxone prior to acupuncture treatment. Wen (1977) successfully used this approach to produce rapid detoxification in heroin addicts using only a single electroacupuncture treatment of 3 to 4 hours duration in combination with pre-administration of naloxone.

The met-enkephalin levels in the cerebral spinal fluid (CSF) of heroin addicts was observed to increase by electroacupuncture (Wen, 1980; 1983) although plasma and CSF levels of beta-endorphin did not change (Wen, et al, 1980). However, beta-endorphin activity in the brain did increase in morphine dependent mice treated for naloxone induced withdrawal using electroacupuncture (Wen, et al, 1979). Inhibitors of the enzymes that breakdown endogenous opiates can potentiate the effect of electroacupuncture indicating a common path between receptors stimulated by opiates and acupuncture

Norepinephrine (NE)

Acupuncture analgesia is also attenuated by an influence on central catecholamines involving alpha receptors (Xie, et al, 1983; Xie, et al, 1985). One of the important actions of cocaine is the ability to block the re-uptake of norepinephrine with the consequence of increasing its level and enhancing the effect on the sympathetic system. This may be very significant in relationship to cocaine's damaging potential to the heart and blood vessels.

Lorenz, et al (1975) observed that plasma catecholamine levels were significantly decreased in morphine dependent rats treated with electroacupuncture for naloxone induced withdrawal.

Table 1. Influence Of Central Neurotransmitters On Acupuncture Analgesia (AA).

<u>ATTENUATES AA</u>	<u>AUGMENTS AA</u>
<ul style="list-style-type: none"> • Decrease 5HT by Cinanserin, PCPA, Pargyline or PCA or 5,6,DHT. • Tolerance or Depletion of 5HT by 5HTP. Repeated Electro Acupuncture. • Block Opiate Receptors By Nalox-Bacitracin, D- one. • Production of Possible AOS by Repeated Electro Acupuncture. Bestatin. • Blockade of ACh Synthesis with Physostigmine, Hemicholine (HC-3). • Stimulate DA or Alpha-Receptors Droperidol, with L-DOPA, Apomorphine or Haloperidol. Clonidine. • Increase Central NE With DOPS. <ul style="list-style-type: none"> • Block Beta-Receptors with Propranolol. • Inhibit Synthesis of PDE With Im-Aminophylline. • Increase Central cAMP. • Decrease PGE with Paracetamol. 	<ul style="list-style-type: none"> • Increase 5HT With Clomipramine. • Increase 5HT with • Increase OLS with Phenylalanine or D-Leucine. • Inhibit Enkephalinase with Thiorphan, Captopril or • Increase in ACh by Neostigmine or Eserine. • Block DA Receptors by Spiroperidol or • Destroy Ascending NE Fibers by 6-OHDA. • Block Alpha-Receptors tolamine. • Increase Synthesis of PDE idazole. • Increase Central cGMP. • Increase Prostaglandin E (PGE) by ICV Injection.

5HT: 5 Hydroxytryptamine (serotonin). 5HTP: 5 Hydroxytryptophan (5HT Precursor). ACh: Acetylcholine. OLS: Endogenous Opiate Like Substances (Enkephalins, Endorphins, Etc.), AOS: Endogenous Antiopiate Like Substances. DA: Dopamine, NE: Norepinephrine, DOPS: Dihydroxyphenylserine (NE Precursor), PCPA: Parachlorophenylalanine(Blocks 5HT Synthesis), PCA: Parachloramphenamine, 5.6DHT: 5.6 Dihydroxytryptamine (5HT Fiber Destruction), 6-OHDA: 6-Dihydroxydopamine (NE Fiber Destruction), PDE: Phosphodiesterase (Degrades cAMP).

Dopamine (DA)

Primarily concentrated in the corpus striatum or basal ganglia system of the brain, this transmitter forms an important feedback control circuit from the substantia nigra (SN) to the dorsal raphe nuclei (NDR). The NDR in turn supplies the SN with 5HT containing neurons. It is thought that the action of cocaine is principally mediated by its effect on DA receptors but its influence on blocking the re-uptake of norepinephrine as noted above may also be of prime importance. Acute injection of morphine will initially increase the synthesis of DA in the rat brain which then produces tolerance to this effect thereby decreasing DA. Opiate abstinence is then associated with an increased synthesis of DA in the CNS and antagonists of DA can exacerbate certain withdrawal responses to morphine. The acute effects of morphine can also be antagonized by DA antagonists probably by accelerating the development of tolerance through the increased levels of DA (See Ramsey, 1977). Antagonist to DA, such as haloperidol, has been shown in a dose dependent manner to block signs of abstinence syndrome of opiates. Acupuncture induced analgesia is also enhanced by the DA antagonists, droperidol, spiroperidol and haloperidol and is attenuated by the agonists L-DOPA, apomorphine and clonidine.

Effectiveness of Acupuncture In Treating Addictions

Abstinence syndrome is characterized by increased metabolism of the different neurotransmitters noted above which are normalized as result of acupuncture stimulation (Sytinsky and Galebslaya, 1981). Homeostatic or corrective mechanisms that are disturbed usually show a phase of unbalanced elevation of sympathetic-adrenal activity. Stimulation of the central catecholamine receptors is probably the most important biochemical mechanism responsible for the disturbance of the vegetative organ functions under abstinence. Plasma levels of catecholamines (Lorenz, et al, 1975), adrenocorticotrophic hormone (ACTH) and cortisol (Wen, et al, 1978) and thyroid stimulating hormone (TSH) (Wen, et al, 1980) have been observed to increase in opiate dependent animal and human subjects during withdrawal syndrome. These levels are shown to decrease along with a corresponding decrease in abstinence symptoms as result of electroacupuncture. A decrease was not observed in non-addicts that were treated. Once detoxification is achieved and withdrawal symptoms are not apparent then electroacupuncture does not produce any further reduction in these parameters.

These studies correlate with the effect that mild electroacupuncture stimulation has on inhibiting sympathetic nervous system outflow (Cao, et al, 1983). Strong electroacupuncture stimulation however produces sympathetic activation indicating that it can induce a stress type reaction. This finding is consistent with several other studies that have shown that strong stimulation can produce stress. Impaired or habituated neuronal circuits or nuclei are basically reactivated by acupuncture stimulation to restore vegetative organ functions that are disturbed in the process of withdrawal syndrome.

The application of acupuncture may be one of the most viable approaches to successfully treating drug and substance addiction. Wen and Teo (1975) for example found that electroacupuncture was twice as effective as methadone in detoxifying heroin addicts. The obvious advantage of acupuncture over using methadone is that the subject is not addicted to another drug to replace the original drug. Many of the early studies achieved poor or confused results (See Tables 2,3,4 and 5) as might be expected in any early research effort because there were considerable variations in the treatment approaches. This included differences in the application of points, duration and number of treatments, frequency of electrostimulation, use of adjuvant drugs, inpatient or outpatient basis and some with or without electrostimulation. Also the criteria of success were varied with some studies taking into account reduction in substance use as a measure of success. Several studies failed to provide any measure of success or perform any follow-up assessment and so these can only be considered as philosophical methodology. Almost all of the studies to date suffer from lack of accurate follow up information perhaps because the difficulty in this task was not properly thought out before the study was undertaken. Despite many of these differences a high percentage of success in some studies indicates perhaps properly applied acupuncture can be a very useful modality in treating drug use. Schwartz (1988) however, reviewed much of this data and concluded that acupuncture is not particularly effective in treating smoking and Crottaux, et al(1983) in a controlled study determined that acupuncture although initially

better was only as good as placebo in the long run. The important question is to determine which of any of the factors in these studies were most significant in leading to a high degree of success so that these can be used to design improved and more successful treatment protocol.

Most early studies that relied on press needles, a small wire thumb tack device which is stuck into points on the auricle, or surgical staples were generally ineffective (Tennant, 1976; Gilby, 1977; Parker and Mok, 1977; Sun, 1982; Fang, 1984). When considering the risk of serious infection due to long duration insertion of these devices (5-10 days) their use for any ailment is questionable. Some researchers that did get significant results using press needles or surgical staples also used other body needle treatments and some with electrical stimulation (Sacks, 1975; Wu, 1980; Kusumi, 1986). Point selections in some studies were poor and when attempting to compare so-called sham and real points or whether the treatment was influenced by expectation, not sufficient information was derived to make accurate determination (Steiner, et al, 1982; Lamontagne and Annable, 1979).

Studies that used the "Lung Point" on the ear or locations near the ear got consistently better results probably because they stimulated a branch of the 10th cranial or Vagus nerve (Wen and Teo, 1977; Wen, 1977; 1980; Patterson, et al, 1984)., Tan, et al (1987) used laser stimulation on the Lung and Shenmen points on the ear and noted that success was a function of the power applied with 2.0 milliwatts (mW) being almost ineffective and 3.0 mW producing significant results. This is probably due to the fact that the lower power levels did not cause sufficient tissue damage to provoke the acupuncture reaction (See Kendall, 1989). The effectiveness of ear points in comparison to wrist or nose points has also been examined (Fang, et al, 1984; Tan, et al, 1987) showing that ear points are more efficacious and highly successful results reported by Olms (1981) by using his specially named point "Tee Mee" could not be confirmed.

Table 4. Summary of Studies Evaluating the Effectiveness of Acupuncture in Treating Opiate and Other Drug Addiction

No. Of Cases	Treatment Schedule	Initial Success %	Follow Up: Months Success %		Point Use:		Freq.	
					Body	Ear	Ref. (Hz)	EA
187	5 Times Over 2 Weeks	61.0			N	S	Low	(1)
18	Staple implant	6.0				S		(28)
9		55.5						(30)
10	3 Times/Day For 3 Days,	20.0			N	N		(21)
	1 Times/Day For 2 Days							
25		36.0	12	20.0	N + D			(31)
35	2 Times/Day For 8 Days		12	51.4	N			(26)
15	20 Treatments				N + D			(33)
19	2 Times/Day For 8 Days	89.5			N			(27)
303			18	5.5			2	
50	1 Time, 3-4 Hours	82.0		52.0	N + D			(29)
300	1-3 Times/Day For 2 Wks		10	5.7	N + D			(32)
130	10 Days NET	98.4	12	80.3			Low	(15)
14	2 to 7 Days	85.7			N			(34)

N: Needle; S: Staplepuncture; NET: Neuroelectric Therapy; D: Adjuvant Drug; EA: Electroacupuncture. References: (26) Wen and Teo, 1975; (27) Shuaib, 1976; (28) Tennant, 1976; (29) Wen, 1977; (30)

Severson, 1977; (31) Lorini, et al, 1979; (32) Wen, 1980; (33) Lorini, et al, 1982; (34) Kroening and Oleson,

1985.

In those studies where treatment was given on contiguous days the results were generally better. Where there was a break in the treatment, such as over a week end some subjects experienced withdrawal symptoms (Tan, et al, 1987). One interesting study conducted by Bullock, et al (1987), with long term chronic alcoholics, treated the subjects in three different phases. The first phase (I) consisted of daily treatments for five days followed by phase II consisting of 3 treatments per week for four weeks and then the last phase (III) involving treatments twice a week over a 45 day period. Ten of twenty seven (37%) of a real point group made it through the treatment program whereas only two of twenty two (7.4%) of a sham point group were successful.

Other alcohol treatment studies that included the detoxification phase reported that subjects had no withdrawal symptoms (Olms, 1984; Lewenburg, 1984). Yang and Kwok (1986) found that electroacupuncture reduced withdrawal symptoms in morphine dependent rats by 85% and certain herbs were 68% effective.

Treatment Protocol

The information derived from the early studies was used to develop highly successful clinical procedures to treat substance addiction. The basic approach in using acupuncture considers both the disturbed vegetative functions as result of abrupt abstinence which provokes withdrawal syndrome and the metabolic detoxification processes. Withdrawal relates mainly to affected neural centers and receptors in the brain and to some extent to receptors in the gastrointestinal system. Metabolic detoxification relates mainly to liver function in breaking down various drugs and substances which are then eliminated from the body via the kidneys and bladder. The detoxification profile of a particular substance then is related to the time it takes to clear the breakdown products from the body. The work of Kao and Lu (1974) show that the frequency of withdrawal symptoms decrease with time which indicates that withdrawal correlates with the time decrease in the metabolic detoxification. The clinical approach then is to match the detoxification and withdrawal profile with the appropriate treatment schedule.

One of the main features in the treatment protocol is that the specific drug or substance is not used again (total abstinence) after the first treatment. In the case of nicotine the subjects are requested to dispose of their unused cigarettes prior to leaving the clinic. They are also asked if there are any in their automobile in which case they are requested to bring them back to the clinic for disposal after the treatment.

Acupuncture stimulation reactivates the inhibited neural centers, however, if a significant level of the substance is still present in the blood, because of the slow rate of metabolic breakdown, the effect of the treatment is transitory. This is because the affected neural areas will again be influenced by the remaining substances to cause re-inhibition which then results in the presentation of withdrawal symptoms. Therefore treatment protocol must consider the time dependent characteristics involved in how long it takes for the metabolic breakdown and clearance of the drug or substance from the body. Treatment is provided daily or more often to keep the affected neural centers reactivated over the time period it takes to eliminate all of the drug or substance.

Nicotine for example, is quickly broken down and eliminated from the body perhaps in only two to four days and a chronic user must keep smoking to maintain the critical blood nicotine level to avoid withdrawal. Some heavy users often awake in the middle of the night with a need to smoke because their blood nicotine levels become uncomfortably low while sleeping since the liver continues to breakdown the nicotine. Because nicotine is readily cleared from the body it can be treated over a relatively short time span. Other substances take a longer time to be eliminated, perhaps seven to ten days and hence the treatment period is correspondingly longer. Also, the opiates such as heroin, methadone, opium, etc, have widespread effects on the many receptors in the brain and body and consequently withdrawal symptoms can be far more severe than other substances and the frequency of treatments is increased to compensate for this aspect of the problem.

Psychological counseling is usually not involved in the treatment approach since it seems that the most important aspect of the problem is to get the user through the detoxification phase without experiencing significant withdrawal misery. Follow up treatments a few weeks after the initial detoxification seem to be important and patients should be advised to make use of local support groups

associated with their particular problem. They also can be provided with other training and education to help cope with other physiological habits and body memory. In addition the subject is always advised to seek immediate treatment if and when uncontrollable urges or cravings for the drug or nicotine occur before the person starts using the substance again. One very critical consideration is that should an individual start smoking again or using the former drug for which they were treated and they decide to be treated once more no criticism is made because the person started using the substance again. Criticizing or blaming the person for failure only serves to attack their self esteem which is already damaged as result of substance addiction. So care is taken to maintain a positive approach in re-treating the individual.

Point Selection

The most basic acupuncture point used in the generally successful detoxification protocols involves Lung 2 located approximately in the center of the lower one third of the cavum concha of the auricle. Its importance derives from the fact that this is the only place on the superficial body where a small branch of the Vagus Nerve (10th Cranial) can be directly stimulated. Lung 1 point on the ear, which is located on the upper one third portion of the cavum concha, also has a small sprig of this nerve. However, a comparison study of almost 500 smokers treated with both Lung 1 and Lung 2 to an equal number using only Lung 2 in the point selection showed no difference in the success of the two groups. In order to minimize the total number of points required for successful treatment, only the Lung 2 location of the Vagus nerve is utilized along with other ear and body points.

Treatment success is enhanced by the application of electroacupuncture and therefore one additional point is required on the ear to provide an electrical pathway to restrict the current flow only to the area of the auricle. The point Shenmen, located at the apex of the triangular fossa, provides this feature and it is also an excellent point based on its known traditional application. Low frequency stimulation seems best which is consistent with the known frequency response of the afferent nerves and brain nuclei. Also, it has been demonstrated that frequencies above 60 to 100 Hz. can produce stress analgesia which is not a desired response in treating addictions.

Other traditional points are used such as the so called "Four Gates" consisting of bilateral use of Hegu (LI4) and Taichong (Liv3), which are located at the motor point of the first interosseous muscles of the hands and feet respectively. These points have a long traditional use in producing profound relaxation and suppression of sympathetic nervous system outflow. The traditional points noted for detoxification properties, such as Fuliu (Kid7) and Zhubin (Kid9) are also used in the case of alcohol and opiate treatment. The use of kidney points is appropriate because in Traditional Chinese Medicine (TCM) the kidneys are considered as the main organ for detoxification. The importance of the Zhubin (Kid9) probably is related to the fact that this point is coincident with the medial motor point of the soleus muscle which means its stimulation will provoke a very profound analgesia in the body since it is a large tonic muscle. Fuliu (Kid7) is located a distance of three finger breaths below point Zhubin.

In the treatment of pregnant individuals only the two points on the auricle (Lung 2 and Shenmen) are used to avoid the risk of inducing labor by using feet and leg points. In addition the point Hegu (LI4) is generally counterindicated in pregnancy. Also, in the treatment of elderly subjects the electroacupuncture tends to produce profound relaxation since most of these individuals are energy (Qi) deficient and so it is advisable to make certain that some other person brings them in for treatment. This can avoid the possible risk of the elderly person falling asleep while driving home. All the other normal restrictions related to needling also apply.

Opiate Treatment Protocol

The potential withdrawal from opiates is quite significant and involves CNS receptors plus those in the gastrointestinal tract. In addition to a wide range of reactions, symptoms can also include cramps, constipation and backache. Pain in the low back will sometimes manifest during the actual treatment and the Chinese "Tuina" massage is applied to the back even though the patient is lying on their back. This is accomplished by reaching under the subject to manipulate the area of the low back. Sometimes the patient is given mild stimulation to the back with a plum blossom needle device after the regular treatment. It may take seven to ten days for the opiates to clear the body to the point where withdrawal is not experienced. Because the symptoms are quite profound, two treatments per day are needed for the first three days followed by daily treatments for three more days (See Figure 4.). The total of nine treatments is provided to match the potential detoxification and withdrawal profile.

The heroin and methadone subjects seem quite apprehensive about being needled, especially on the ears, since most are on the verge of abstinence syndrome when they arrive in the morning for the first treatment on the first day. In this situation the four points on the hand and feet (Hegu and

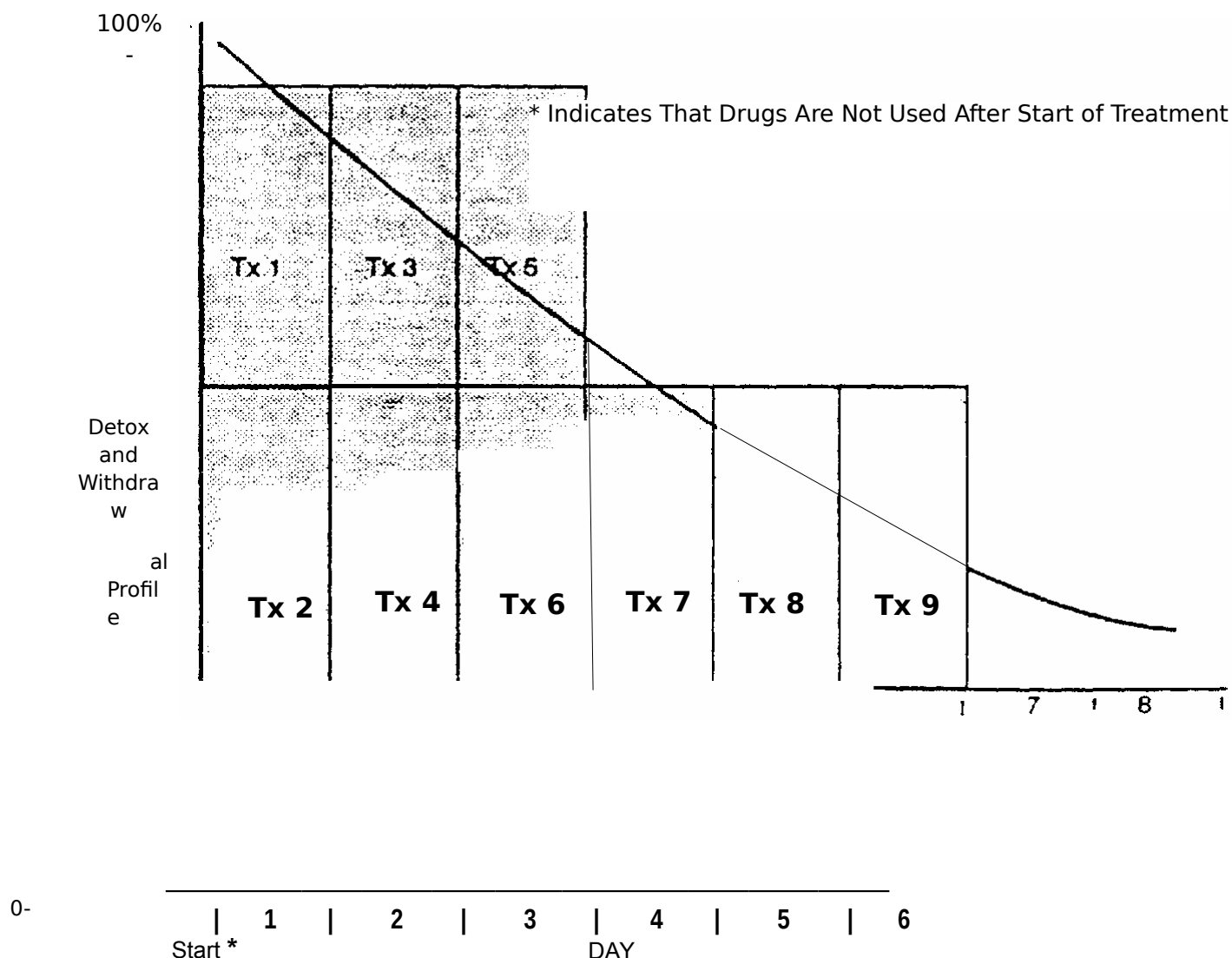


Figure 4. Detoxification and Withdrawal Profile for Opiates and Similar Drugs with Overlay Representing Nine Treatments (Tx) Over Six Consecutive Days

Taichong) are inserted first followed by Zhubin and Fuli on the leg. After this the patient starts to relax and then the two ear points (Lung 2 and Shenmen) can be inserted. Electroacupuncture stimulation is first applied on Zhubin to Fuli, ipsilaterally on each leg. for about 15 minutes duration prior to providing stimulation on the ear points. The ear points are stimulated for an additional 30 minutes, making the total duration of 45 minutes. [**Frequency:** 2 Hz. (Continuous Mode).]

Treatment usually always starts on a Monday morning and the patient is almost always scheduled first or even sometimes early before regular clinic hours. The reason for this is that the subject has not had any drugs since the night before and when they arrive at the clinic they are starting to feel signs of withdrawal. The second treatment is nominally scheduled for mid to late afternoon, however, since there is no way to predetermine how long the patient can go before withdrawal discomfort starts. The patient is advised that even though they have a nominal appointment for the second treatment that day they should come in immediately should they feel they can not wait for the scheduled time slot. For an outpatient treatment protocol, one should be aware that the opiate addict will usually show up quite early for the treatments on subsequent days.

As noted above, two treatments, one in the early morning and one in late afternoon are provided for the first three days. One treatment each morning is then provided for the next three days.

Occasionally a third treatment is provided on the first day although almost all make it through with the scheduled two. Also, on occasion a patient may require two treatments on the fourth day, but this is usually rare. Some treatment approaches for inpatient care involved staying with the addict and providing treatment whenever abstinence symptoms presented (Kao and Lu, 1974). Single follow up treatments are essential for opiate addicts, usually scheduled at one, three and six weeks after completing the first course of treatments. It seems that former addicts have poorer coping skills to handle subsequent stress exposure. Therefore they are encouraged to seek treatment when stress is high.

One interesting observation about opiate addicts is that often they do not want to pay for their treatments or they try to find a way of not paying, such as writing bad checks. Whether this observation is related to long time behavior patterns of surviving with opiate addiction is not known.

Treatment and Schedule for Heroin, Methadone and other Opiates

Auricular Points: Shenmen, Lung 2.

Body Points: Hegu (LI4), Taichong (Liv3), Zhubin (Kid9), Fuli (Kid7)

Electroacupuncture: Zhubin (Kid9) (Positive) to Fuli (Kid7) (Negative) ipsilaterally on each leg for 15 minutes duration and then change application to the ear from Shenmen (Positive) to Lung 2 (Negative) ipsilaterally on each ear for an additional 30 minutes.

Frequency: 2 Hz. (Continuous Mode).

Duration: 45 Minutes.

Schedule: Two treatments each day for first three days and then one treatment each day for an additional three days (nine treatments over six consecutive days)

Follow Up: A single follow up treatment is advisable at the end of 1, 3, and 6 weeks after the first course of treatments. Subject should be advised to seek acupuncture treatment anytime that strong urges or uncontrollable craving to use drugs occur prior to actually taking the drugs. Should the subject inadvertently use drugs or be coerced into trying drugs, they should be advised to immediately come in as soon as possible for one (1) or more follow up treatments.

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V. Other Strategies to Support Continued Sobriety

This section is pretty simple. Encourage your patients to attend meetings of Alcoholics Anonymous (AA) or Narcotics Anonymous (NA) and have their friends and family members attend Al-Anon. These groups charge no money but accept voluntary contributions. The confidentiality and anonymity of all who attend are respected, and the groups do truly miraculous work with those in attendance. The meetings address the spiritual aspects of the disease of addiction and offer those who attend a very special kind of love, understanding, and support.

To find Alcoholics Anonymous groups in your area, search: <http://www.aa.org/>
Many who suffer from narcotics addictions benefit by attending AA meetings.

To find Narcotics Anonymous groups in your area, search:
<http://www.naws.org/meetingsearch/>

To find Al-Anon groups in your area, search" <http://www.al-anon.alateen.org/>
Al-Anon offers strength and hope for friends and family members of problem drinkers and drug abusers.

V. Other Strategies to Support Continued Sobriety

A. Supporting Dopamine Activity, Response, and Synthesis in the body

From the acupuncture research presented in the previous section and from the protocols of Dr. Deke Kendall, it is very apparent that 2 Hz Electro-Acupuncture (EA) stimulation increases dopamine production, and that dopamine is the key neurotransmitter needed by those undergoing opioid withdrawal and for those who want to maintain continued sobriety.

Dr. Kendall's observation on dopamine (DA) is well worth repeating:

“Opiate abstinence is then associated with an increased synthesis of DA

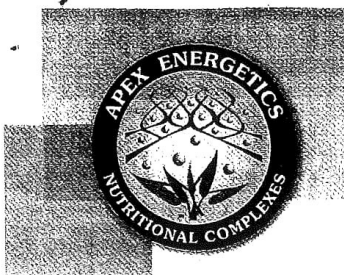
in the CNS and antagonists of DA can exacerbate certain withdrawal responses to morphine.”

Perhaps Dr. Lauren Laks' Xuan Xia Detox Formula also supports dopamine synthesis. In my own experience, providing nutritional supplementation which supports dopamine activity, response, and synthesis in the body helps those withdrawing from opioids and those working to maintain their sobriety.

I use a product from Apex Energetics called Dopatone. Again, I have NO financial relationship with Apex Energetics and derive NO financial gain for the promotion of its product, Dopatone.

<https://www.amazon.com/Apex-Energetics-Dopatone-K-41-Capsules/dp/B007RPUJJI>

What follows is Apex's product information for Dopatone



K41

DOPATONE[®] ACTIVE

Supports Healthy Dopamine Response, Activity, & Synthesis

BENEFITS OF PRODUCT

- Provides amino acids and cofactors required for dopamine production.
- Provides phytonutrients that exhibit/support dopamine activity.
- Provides phytonutrients that have shown to protect dopaminergic neurons.

USE OF PRODUCT

To help support healthy Dopamine levels as it relates to nutritional balance.

OTHER PRODUCTS TO CONSIDER

Other products can be used in conjunction with Dopatone[®] Active to balance Dopamine. Apex's Sublingual Vitamin-B12 (K34) is a rich source of micronized methylcobalamin that can provide essential methyl compounds to support neurotransmitter balance. Stress responses can cause neurotransmitter imbalance. Adaptocrine[®] (K02) can be used to provide stress adaptogens to support healthy neurotransmitter levels. Adrenacalm[™] (K16) provides a rich source of liposomal phosphatidylserine which can be useful in the same manner.

KEY INGREDIENTS RESEARCH COMMENTARY

The research information presented here should not be construed as claims regarding performance of this product.

MUCUNA PRURIENS is commonly known as cowhage and its active components include L-Dopa, tyrtamine alkaloids, lecithin, and tannins. It is postulated that the L-Dopa amino acid compounds in the botanicals are converted into dopamine in the brain. It has been used as a botanical for neurological disorders since ancient days and recent research has demonstrated that the botanical has Anti-Parkinson influences due to its precursor compounds. Additionally, the active components in Mucuna pruriens have protective impacts on the substantia nigra and nigrostriatal pathways.^{1,2,3,4,5,6}

BETA-PHENYLETHYLAMINE (PEA) is an endogenous monamine alkaloid and crosses the blood-brain barrier easily. It acts as a neuromodulator in the nigrostriatal dopaminergic pathway and stimulates the release of dopamine. PEA also has influences on beta endorphins that have been attributed to feeling of pleasure. Chocolate contains a rich source of PEA and it is this mechanism that is theorized to cause the feelings of love, pleasure, and satisfaction via dopamine activation. PEA supplementation has shown to improve attention and enhance mood.^{7,8,9,10,11}

BLUEBERRY EXTRACT contains a rich and potent source of antioxidants, particularly the Anthocyanin compounds. These compounds have proven effective in free radical quenching areas of the dopamine-rich neurons of the central nervous system.^{12,13,14,15}

Supplement Facts

Serving size 1 vegetarian capsule
Servings per container 90

Amount Per Serving	% Daily Value	
Vitamin B6 (as pyridoxal 5 phosphateate)	10 mg	500%
Selenium (as selenomethionine)	25 mcg	35%
Mucuna Pruriens extract	300 mg	*
D,L-Phenylalanine	200 mg	*
Beta-Phenylethylamine	80 mg	*
N-Acetyl L-Tyrosine	100 mg	*
N-Acetyl L-Cysteine	100 mg	*
Blueberry extract (fruit)	25 mg	*
Alpha Lipoic Acid	10 mg	*

*Daily Value not established

Other ingredients: Vegetable cellulose (vegetarian capsule), silicon dioxide.

DIRECTIONS

Take 1-2 capsules, 3 times a day, or as directed by your healthcare professional.

D, L-PHENYLALANINE (DLPA) is an essential amino acid precursor for the production of dopamine. It is required from the diet from sources such as meat, fish, eggs, and dairy products. The L-form of phenylalanine is converted into catecholamines such as dopamine. The D-form of phenylalanine is used to produce the dopamine modulator phenylethylamine. The combination of both forms of phenylalanine are referred to as DLPA and found to be an effective mood enhancer, and reduce pain perception. DLPA prevents the breakdown and degradation of endorphins.^{16,17,18,19,20,21}

This product is not intended for use as a replacement for medications prescribed by a medical doctor. Intended for nutritional purposes only.

Statements in this flyer have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Formula Info Page



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N-ACETYL-TYROSINE is an amino acid that serves as a precursor for dopamine production. Oral supplementation with tyrosine results in increased plasma and brain levels of the compound. Tyrosine supplementation has demonstrated the ability to change plasma neurotransmitter levels. Tyrosine is converted into dopamine by the enzyme tyrosine hydroxylase in the brain. Additionally, tyrosine depletion by dietary means produces symptoms of decreased dopamine in both human and animal studies.^{22 23 24 25 26 27}

PYRIDOXAL-5-PHOSPHATE (P-5-P) the active form of vitamin B6 is pyridoxal-5-phosphate (P-5-P) and undernutrition of²⁸ this compound promotes loss of dopamine in the corpus striatum. It appears that dopaminergic neurons of the nigrostriatal tract may be vulnerable to long-term P-5-P deficiency. Additionally, P-5-P deficiency prolongs the time course of evoked dopamine release from the rat striatum.^{29 30 31 32}

GLUTATHIONE COFACTORS The substantia nigra is extremely sensitive to oxidative stress by hydroxy radicals. Glutathione has demonstrate promise in protecting these neuronal tissues responsible for producing dopamine. The essential nutritional substrates for the synthesis of glutathione are selenium, and N-acetyl-cysteine.^{33 34 35}

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B. Twelve Step Programs

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