

Affective Disorders, Monoamine Oxidase and Chinese herbs

An affect disorder is any pathological condition of mood, which interferes with normal cognitive and emotional functioning as well as having strong physiological effects. Depression and anxiety are the most common categories of affective disorder. Depressive and anxiety disorders are common, occurring in up to 25% of primary care patients, (1) and are more disabling, both socially and in terms of physical functioning, than many chronic physical illnesses, such as diabetes, hypertension, and arthritis and back pain. (2,3)

The most thorough large-scale study is the World Health Organization [WHO] study on psychological disorders in primary care. (1) Over 25 000 consecutive adults were screened at 15 sites in 14 countries. Over 5 000 were further assessed with detailed psychiatric interviews. A quarter had a recognisable mental disorder, the commonest being a depressive disorder; 11.7% or an anxiety disorder; 10.5%, with 4.6% having both. Only half of the mental disorders were recognised by the primary care physician; among those patients with a recognised mental disorder, half were offered drug treatment.

A similar study in Australia of 4867 patients of 117 general practitioners found that 35.6% had elevated scores on a screening test for mental illness, while 20.6% had been treated for anxiety or depression in the previous 12 months. (4)

NIMH (National Institute of Mental Health; US) research has revealed that depression often co-exists with anxiety disorders (panic disorder, obsessive-compulsive disorder, post-traumatic stress disorder, social phobia, or generalized anxiety disorder). Depression, stress and anxiety have a common cause as the body raises cortisol levels and activates monoamines in response to perceived danger, which alter neuroendocrine transmitters.

Depression

The symptoms of depression include persistent sad mood; loss of interest or pleasure in activities that were once enjoyed; significant change in appetite or body weight; difficulty sleeping or oversleeping; physical slowing or agitation; loss of energy; feelings of worthlessness or inappropriate guilt; difficulty thinking or concentrating; and recurrent thoughts of death or suicide. Clinical depression is diagnosed when there are at least three or four symptoms present every day for at least two weeks.

Anxiety

Anxiety is characterized by a sense of agitation and impending doom; sleep disturbance, palpitations and being easily startled. There is also a constant worry and fretting.

Anxiety disorders can be triggered by a number of factors, including life experiences, psychological traits, and occasionally other disorders such as sleep disorders and depression. Family history and genetics also play a part in the likelihood of someone having an anxiety disorder. Increased stress and inadequate coping mechanisms to deal with that stress may also contribute to anxiety.

There is a link between anxiety disorders and an imbalance in certain neurotransmitters in the brain, which regulate anxiety. The areas of the brain implicated in anxiety are the forebrain and the limbic system. The forebrain is the area most affected in people with

anxiety disorders. The limbic system is involved in storing memories and creating emotions and is thought to play a central role in processing all anxiety-related information. Both the locus coeruleus and the dorsal raphe project to the septohippocampal circuit, which in turn projects to other areas of the limbic system that mediate anxiety. The hippocampus and amygdala are of particular importance in that they are interconnected and also project to both subcortical and cortical nuclei. The noradrenergic and serotonergic systems are also involved in controlling anxiety and are almost certainly involved in the pathogenesis of anxiety disorders.

Neuroendocrine Abnormalities

Many depressed and / or depressed patients also have neuroendocrine abnormalities, they produce large amounts of cortisol, and they are unable to cut down this excessive cortisol production when given dexamethasone. Investigators have also observed other types of failure in neuroendocrine modulation and secretion. Depressed patients failed "insulin tolerance test", thyrotropin-releasing hormone (TRH) test and others.

The pattern of abnormality suggests that the defects do not lie in target organs, such as the adrenals or thyroid, or even in the pituitary gland itself. Rather, they are probably at the level of the hypothalamus, the command centre governing the pituitary, or at some even higher level. Messages sent from other parts of the brain to the hypothalamus usually use the norepinephrine system. Likewise, dopamine and norepinephrine are the neurotransmitters used by the hypothalamus to talk to the pituitary. It is therefore possible that all the neuroendocrine abnormalities in depression could be explained through the catecholamine hypothesis - that is, depressed patients have a defect in norepinephrine transmission that impairs their ability to regulate the secretion of all types of hormones. In accordance with the monoamine hypothesis, a deficit in brain norepinephrine and dopamine exists in patients with depressive illness. (5,6) Further, there exists a theory that there are two types of depression. Low levels of the catecholamines Dopamine (DA) and Norepinephrine (NE) are associated with Type-A, while low levels of serotonin (5-HT) are associated with Type-B depression. (7)

Brain Abnormalities

In some people with post-traumatic stress disorder, the hippocampus appears to be smaller. This may be due to the degeneration of dendrites in this part of the brain, which is caused by a stress-induced increase in the concentrations of glucocorticoids (cortisol). Other brain structures involved in controlling emotion, such as the hypothalamus, may also be involved in the pathogenesis of anxiety disorders. People with obsessive-compulsive disorder often show increased activity in the basal nuclei, particularly the striatum, and other frontal lobe. Several neurotransmitters, including noradrenaline, serotonin, and GABA, cholecystinin and corticotropin releasing factor appear to be involved in anxiety disorders and may contribute to the symptoms of the disease.

When we examine the neuro-endocrinological patterns in depression and anxiety we can see a clear imbalance in a number of brain functions, particularly the hypothalamus-pituitary-adrenal (HPA) and hypothalamus-pituitary-thyroid (HPT) pathways, which are responsible for managing stress. There is also a corresponding deficiency in the immune system due to the elevation of cortisol, an increased likelihood of Chronic Fatigue Syndrome.

Hypothalamic-Pituitary-Adrenal (HPA) axis

Abnormalities in the Hypothalamic-Pituitary-Adrenal (HPA) axis have been found in about 50 % of the depressed patients in the acute phase using the dexamethasone suppression test (DST). To further test HPA-axis disturbances in depression, the release of adrenal corticotropin (ACTH) after administration of corticotropin-releasing hormone (CRH) was studied in 24 depressed patients, in relation to the DST. After CRH-stimulation significantly lower cortisol and ACTH levels were found for DST-non-suppressers compared to DST-suppressers.

In a sample of 28 depressed patients, over a 15-year observation period, different statistical and clinical clusters were identified. Examination of 45 variables, tested using Principle Component Analysis (PCA), revealed that the three biological variables, including platelet monoamine oxidase activity (MAO), peak nocturnal serum melatonin and maximum post dexamethasone cortisol, and the two clinical psychomotor symptoms; Reduced speech and slowness of movements, contributed most to the clustering of individuals. (8)

Hypothalamus, Hippocampus and the Amygdala

The hypothalamus, the brain region responsible for managing hormone release from glands throughout the body, increases production of a substance called corticotropin releasing factor (CRF) when a real or imagined threat to physical or psychological well being is detected. Elevated levels and effects of CRF lead to increased hormone secretion by the pituitary and adrenal glands, which prepares the body for defensive action. The release of cortisol prepares the body for fight or flight and when we neither fight nor flee, the cortisol can actually begin to destroy the brain and impair thinking. The body's response to cortisol includes reduced appetite, decreased sex drive, fatigue and panic.

NIMH research suggests that persistent over-activation of this hormonal system may lay the groundwork for depression and anxiety (9).

The HPA axis is working overtime during these stressful situations, and new studies have suggested that two areas of the brain responsible for kicking this axis into action:

The hippocampus and the amygdala are two key regulatory centres located in the cerebral areas of the brain, governing memory storage and emotions, respectively. Both are major nuclei of the limbic system, which underlies emotions.

Stress can lead to neuronal loss and atrophy in the hippocampus, which is reduced in depressed patients.

The hypothalamus and the pituitary gland may also play a role in depression, as they are involved in hormonal control, and increased levels of some hormones may play a role in maintaining a depressed state.

Summary

When the body is placed under stress, the hypothalamus-pituitary-adrenal axis becomes activated. The hypothalamus produces corticotropin releasing factor (CRF), which is hypothesised to play a role in the precipitation of certain forms of depression. CRF stimulates the pituitary gland to secrete adrenocorticotrophic hormone (ACTH), which in turn stimulates the adrenal glands to release cortisol. Cortisol depresses mood, lowers immune and sexual functions, and activates monoamine oxidase. Approximately 50% of people with severe depression have raised cortisol levels.

Monoamines, Monoamine Oxidase and Monoamine Oxidase Inhibitors

The monoamine theory suggests that depression is caused by a deficiency in monoamine-dependent neurotransmission. This theory was first developed in the 1950s, following the observation that treatment with the drug reserpine (antihypertensive drug; no longer available in many countries) could induce depression. It was found subsequently that the mechanism of action of reserpine was to deplete neurons of their monoamine neurotransmitters such as serotonin and noradrenaline (10). Arguably, this situation would result in a shortage of monoamines, so preventing or reducing neurotransmission in serotonergic or noradrenergic neurons.

This hypothesis in its simplest form, stated that depression was due to a deficiency of norepinephrine, one of the major catecholamine systems in the brain. The catecholamine theory received some support as the mechanisms of the new antidepressant drugs were illuminated. Both types of drugs used to treat depression, the tricyclics and the monoamine oxidase inhibitors (MAOIs), tend to increase the amount of norepinephrine available in the central nervous system, although they work in somewhat different ways.

The MAOIs block the action of monoamine oxidase, thereby preventing norepinephrine from being destroyed and increasing the amount available for transmission. (11)

The main role of MAO in the brain is to break down several neurotransmitters such as noradrenaline, dopamine and 5-HT- the chemicals that nerve cells use to communicate. Neurotransmitters are the central constituents of emotion, perception and thought.

MAO A & B

MAO A deals primarily with serotonin, dopamine and norepinephrine, while MAO B mainly breaks down phenyl ethylamine. MAO exists in two similar molecular forms, coded by separate genes. MAO-A has a substrate preference for 5-HT and is the main target for antidepressants. MAO-B has a substrate preference for phenylethylamine

"This tells us that anxiety and aggression are regulated by similar neurotransmitter pathways," said Shih, noting that this may bear importantly on the fact that some antidepressants work by specifically targeting MAO production. (11)

MAO is under heavy genetic control (12) and is influenced by sex and stress hormones (13) specifically the sex hormones progesterone, oestrogen, and androgen affect MAO levels. Progesterone has been shown to increase MAO activity. Oestrogen and androgens both decrease MAO activity (13). Symptoms of these reactions can be seen in humans. When women ovulate they produce excess levels of oestrogen, which will inhibit MAO activity, which may be related to PMS. Responses to hormones were further confirmed with experiments with lab animals. These experiments have shown that when a male is castrated following puberty, it causes their MAO activity in the brain to rise. Then when they gave these animals an injection of exogenous testosterone causes they found it lowered the activity of the enzyme.

Hormones released during stress also affect MAO activity. Hormones released during stress include epinephrine and corticosterone. These hormones appear to depress MAO activity.

Conclusion

Firstly, stress, sexual activity and age all affect monoamine oxidase. While on a purely mechanical level, stress and certain sexual hormones depress MAO activity this does not take into account the long term changes that occur in the HPA and HPT pathways which appear to become non-responsive to their own feed back mechanisms.

Secondly, MAO A and MOA B appear to be involved in different feedback mechanism in response to stimulation. MAO A and MOA B destroy small molecule neurotransmitters but leave open the question of regulation of cGMP and cAMP neurotransmitters.

Simply said, MAO A activity may create anxiety while MOA B activity may be involved in depressive states. There is quite likely a *YIN* or *YANG* affect associated with MAO A or B activity with the distinct possibility of the conversion of one state to another.

Chinese herbs have *YIN* or *YANG* qualities and MOAI herbs can be prescribed for anxiety, depression (uni or bi polar) and agitated (suicidal) depression according to their actions. Chinese research as back as the late 50's indicate that Kidney Yin and Kidney Yang Xu are related to adrenal cortex imbalance. (14)

MAO-inhibiting herbs

Lu Rong

Within 6 days, accelerated aged mice and normal mice were given Lu Rong extract via p.o. once every day, and the MAO-B in the liver and brain tissues of mice was obviously inhibited. In vitro experiments further confirmed that normal butyl alcohol and ether extract of Lu Rong inhibited MAO activity, and the main active ingredient in the normal butyl alcohol extract that could inhibit MAO activity was hypoxanthine. Though uracil could also inhibit MAO activity, its strength was obviously lower than hypoxanthine. At the concentration of 10~640_l/ml, the inhibitory effect of hypoxanthine on MAO activity was parallel to its concentration, and its inhibitory effect on MAO-B was greater than on MAO-A. 18 months old aged mice was given 200mg/kg of hypoxanthine via p.o. once every day within six days, and the activity of MAO-B in the mice brain could be obviously inhibited, meanwhile, the content of monoamines (such as 5-HT and noradrenalin) in the brain tissue was increased.

—Wang Benxiang, et al. *Review of the chemical, pharmacological and clinical research on Lu Rong. Acta Pharmaceutica Sinica, 1991; 26(9): 714~720*

Lu Rong extract had obvious inhibiting effect on MAO-B activity in the brain and liver of senile mice, but it had no obvious influence over MAO-A. It could significantly increase 5-HT, NE and DA contents in the brain of senile mice. In vitro experiments proved that on MAO-B, Lu Rong extract had competitive inhibition action; while on MAO-A, it had mixed inhibition action.

—Chen Xiaoguang, et al. *Research on MAO-inhibiting action of Lu Rong extract in senile mice. Journal of Chinese TCM, 1992, 17(2): 107~110*

Senile mice (15 months old) were given Lu Rong total fat (1~2g/kg) through gastrogavage for 8 days in succession, its inhibiting effect on the activity of MAO-B was obviously stronger than that on young mice (1 month old) treated with above method, while the inhibiting effect

on the activity of MAO-A was similar to that on young mice; and in the brain tissue, the inhibiting effect on MAO-B activity was stronger than on MAO-A. In addition, gastrogavage of Lu Rong total fat in succession could significantly inhibit the MAO activity in the brain of senile mice (18 months old), and increase the contents of monoamine substance DA and 5-HT in the brain as well. In vitro experiments proved that Lu Rong total fat had obvious inhibiting effect on the activity of MAO-B, but its inhibiting effect on MAO-A was not obvious. This study indicated that Lu Rong had anti-aging effect.

—Chen Xiaoguang, et al. *Inhibiting effect of Lu Rong total fat on MAO. Chinese herbal medicine, 1990; 21(11): 21~24*

Research showed that Lu Rong extract had obvious inhibitory effect MAO-B activity in the brain and liver of both senile mice (20 months old) and young mice, and this MAO inhibiting effect was more obvious in senile mice than in young mice. It had no obvious influence over MAO-A. Aqueous extract of Lu Rong at the dosage of 0.5g/kg had no significant influence on monoamine transmitters in the brain of mice; at the dosage of 1.0g/kg, it could obviously increase the contents of monoamine transmitters (5-HT, NE, DA) in the brain of senile mice ($P < 0.05$). Though the contents of monoamine transmitters in the brain of young mice increased, there was no statistical significance. In vitro experiments showed that Lu Rong extract had competitive inhibition action on MAO-B and mixed inhibition action on MAO-A. When the warm incubating time was 30 minutes, and the enzyme concentration was 200_g/ml, the MAO-inhibiting effect of Lu Rong extract was the highest.

Further research proved that both normal butyl alcohol and ether extract of Lu Rong could inhibit MAO-B. Through the research on hypoxanthine which was one of normal butyl alcohol extracts and Lu Rong phospholipid which was one of the chloroform extracts, it was found that both hypoxanthine (50~500mg/kg) and Lu Rong phospholipid (200~800mg/kg) had an inhibitory effect on MAO-B activity in the liver and brain of mice, but the effects on MAO-A were not obvious. They showed competitive inhibition action on MAO-B and mixed inhibition action on MAO-A. When the dosage of hypoxanthine through Po or Sc was over 50mg/kg, its inhibitory rate on MAO-B in the liver and brain were more than 50%, and the inhibitory effect was the strongest 16 hours after the administration. The MAO-B inhibiting time could last 72 hours through Po administration. The strength of MAO activity inhibiting effect aroused by the same dosage of hypoxanthine through Sc administration was not as good as that of Po administration, and the acting time was less. Lu Rong phospholipid had quite strong inhibitory effect on MAO-B activity. With the increasing of concentration, its effect increased too, but when the concentration was over 2.0mg/kg, the inhibitory effect on MAO-B reached maximum.

—Zhou Qun, et al. *Review on MAO-inhibiting effect of traditional Chinese medicine. Chinese pharmacy, 1995; 6(2): 41~42*

Dang Gui

Dang Gui injection was administrated to mice at different dosage through gastrogavage, once every day for 4 weeks. This treatment significantly lowered the activity of MAO-B in the brain and liver of mice. The result indicated that Dang Gui injection could delay ageing.

—Zhang Mingyuan, et al. *The influence of Dang Gui injection over the activity of MAO-B in the brain and liver of senile mice. Learned journal of Jimusi medical college, 1997; 20(4):10~11*

Dong Chong Xia Cao (Cordyceps)

In this study, radioactive isotope method was used to observe the influence of 3 kinds of mycelia of Cordyceps over MAO-B activity of rats and mice. The results showed that three kinds of mycelia of Cordyceps all had significant inhibitory effect on the activity of MAO-B in the brains of rats and mice. When the concentration was 1:1, its inhibitory effect over MAO-B was over 70%; while the drug concentration was 1:10, the inhibitory effect over MAO-B was over 30%.

—She Min. *The influence of mycelia of Cordyceps over MAO-B in the brains of mice and rats. Chinese traditional and herbal drugs. 1991; 22(5): 218~219*

Gan Cao

In this study, Wistar rats were used as the experimental subjects, and their activity of SOD in RBC, activity of MAO-B in the brain tissues, as well as content of LPO in RBC were determined. The changes of the above-mentioned indices following age, and the influence of Gan Cao over above-mentioned indices were observed. The results showed that the activity of SOD in rats increased with the increasing of age in their growth stage ($P<0.01$), the content of LPO in RBC increased with the increasing of age, and the activity of MAO-B in the brain tissues increased with the increasing of age. Water decoction of Gan Cao could increase the activity of SOD, lower the content of LPO and lower the activity of MAO-B in senile rats ($P<0.01$). There's no significant difference in the influence of different administration time over above-mentioned indices. The results indicated that Gan Cao could delay ageing.

—Wang Chao, et al. *Experimental research on the influence of Gan Cao over SOD, LPO and MAO-B in senile rats. Chinese journal of gerontics, 1998; 18 (6): 371~372*

Ge Jie

Ge Jie had significant inhibitory effect on MAO-B in rat brain ($P<0.01$); meanwhile, it could also obviously lower the concentration of FSH ($P<0.05$), and significantly increase the concentration of estradiol in the blood of rats. The author believed that Ge Jie could obviously improve the function of the hypothalamus-pituitary-gonad axis.

—Zhou Xiaomian, et al. *The influence of Ge Jie over MAO-B in the brain of rats and FSH & estradiol in blood. Learned journal of No. 1 Military Medicine University, 1994, 14 (1):42.*

He Shou Wu

In this study, Wistar rats were used as the experimental subjects, the influence of extract liquid of prepared Shou Wu over the activity of MAO-B in the hypothalamus, pons and whole brain, as well as the influence over the content of LPO in the liver was studied. The results showed that: prepared Shou Wu had significant inhibitory effect over the activity of MAO-B in the hypothalamus, pons and whole brain, it also could lower the content of LPO in the liver. The results indicated that prepared Shou Wu had certain anti-ageing effect.

—Ding Wei, et al. *The influence of prepared Shou Wu over MAO-B in the hypothalamus and pons and LPO in the liver of senile rats. Journal of gerontics. 1993; 13(5):306~307.*

In this experiment, the influence of different kinds of extract liquid of Shou Wu (alcohol extract or aqueous extract) over the changes of SOD, LPO in the heart, liver and brain as well as MAO-B in the brain of senile rats was observed. The results showed that two kinds of extract liquid of Shou Wu could to different degree increase the content of SOD in the tissues, lower the content of LPO. Aqueous extract of Shou Wu could also lower the activity of MAO-B in the brain. The results indicated that different kinds of extract liquid of Shou Wu could increase the ability of clearing superoxide free radicles by means of exerting influence over the defence enzyme-SOD, or delay ageing by means of inhibiting the activity of MAO-B in the brain of rats.

—Han Zhifen, et al. *The influence of different kinds of extract liquid of Shou Wu over free radicle metabolism and MAO-B in the brain of senile rats. Chinese medicine science and technology of China. 1995; 2(2): 36~37*

Senescence accelerated mice were given alcohol extract of He Shou Wu through gastrogavage for 5 days in succession, and the activity of MAO-B in the liver and brain was significantly inhibited. But this method showed no effect on the activity of MAO-A.

—Yang Xiuwei. *The influence of alcohol extract of He Shou Wu over the activity of MAO in the liver and brain of senescence accelerated mice. Journal of Chinese Medicine of China, 1996; 21 (1): 48~49*

Ji Xue Teng

In this study, male mice weighting from 20~26g were used as the experimental subjects, and the MAO-A activity inhibiting effect of Ji Xue Cao (Herba Centellae cum Radices) extract over in vitro brain of mice was studied. The results showed that three extracts of Ji Xue Cao could all significantly inhibit the activity of MAO-A of in vitro brain of mice in a dose dependent manner, and the inhibitory effect of 50% alcohol extract was the best. This result indicated that Ji Xue Cao may have anti-depression effect.

—Zhang zhongqi, et al. *The MAO-A activity inhibiting effect of Ji Xue Cao extract over in vitro brain of mice. Bull. Acad. Mil. Med. Sci. 2000; 24(2): 158.*

Jiao Gu Lan

This article studied the effect of gypenosides on MAO and Na/K-ATPase activities in brain tissues of aging mice. In the study, models of aging mice were prepared by continuous post-orbital injection of 120mg/kg D-galactose for a month, then the effects of gypenosides on MAO and Na/K-ATPase activities in brain tissues were investigated. It was found that MAO activity was increased and Na/K-ATPase activity was decreased in brain tissues of aging mice models significantly; and these effects were reversible respectively by gypenosides ig at the dosage of 75 and 150mg/kg. The result that gypenosides could invert the changes of MAO and Na/K-ATPase activities in brain tissues of aging mice, may provide a further explanation of the anti-ageing mechanism of gypenosides in molecule enzymology.

—Gong Guoqing, et al. *Effects of gypenosides on monoamine oxidase and Na/K-ATPase activities in brain tissues of aging mice. Chinese traditional and herbal drugs, 2001; 32(5):426~427*

Ling Zhi

Fermentation liquid of Ling Zhi and superoxidized oil were administered to mice through gastrogavage to observe its influence over lipid peroxidation, lipofuscin in the brain and heart, SOD in the serum and activity of MAO in the brain. The results showed that fermentation liquid of Ling Zhi could increase the activity of SOD of mice, decrease the generation of MDA in the serum, inhibit the generation of lipofuscin in the heart and brain, and lower the activity of MAO in the brain as well. The results indicated that fermentation liquid of Ling Zhi had certain anti-ageing effect.

—Hu Xiaoping, et al. *Experimental research on anti-ageing effects of fermentation liquid of Ling Zhi. Practical preventive medicine, 1997; 4 (2): 65~66*

Ren Shen

Research showed that ginsenoside had significant inhibitory effect on the activity of MAO, and it's believed that it's a kind of inhibition of non-competitive type, which was proved in in-vitro experiment with cytochemical methods. It's believed that in vitro, the content of MAO was positively correlated to the occurrence and development of the ageing of human embryon lung or fibrocyte, and SRG/ SFG and SSLG could all obviously lower the content of MAO in cells of high generation; SRG and SSLG could also inhibit MAO in cells of early generation.

The influence of SSLG and its monomers of Rg₁, Rg₂, Re and Rh over the activity of MAO-B in the brains of mice was studied with in vitro methods. The experiment showed that SSLG and Rh could increase the activity of MAO-B, Rg₁ and Rg₂ could inhibit the activity of MAO-B, and its inhibitory strength was similar to that of 3.3×10⁻⁵mg/ml cutonyl, and the inhibitory rate was 20~30%. Re had no obvious influence over the activity of MAO-B. The curve of inhibitory characteristics showed that the inhibitory effect of Rg₁ and Rg₂ over MAO-B was competitive.

—Zhou Qun, et al. *Review on MAO-inhibiting effect of traditional Chinese medicine. Chinese pharmacy, 1995; 6(2): 41~42*

Others herbs

The observation on the influence of qi-invigorating & yang-warming medicines over the content of catecholamine neurotransmitters and the activity of MAO-B in the hypothalamus of rats showed that: compared with normal rats, in the rats of cortisone-induced yang deficiency model, the contents of dopamine (DA) and noradrenaline (NA) lowered (P<0.05, P<0.01); the activity of MAO-B increased (P<0.05). Qi-invigorating and yang-warm medicines or single application of yang-warming medicines could increase the NA content and inhibit the activity of MAO-B in the hypothalamus of rats of cortisone-induced yang deficiency model, and compared with the model group, P<0.05 or 0.01. Single application of qi-invigorating medicine had no obvious influence over above indices.

—Zheng Bing, et al. *The influence of qi-invigorating & yang-warming medicines over the content of neurotransmitter and the activity of MAO-B in the hypothalamus of rats. Hunan Journal of TCM, 1997; 13(1): 45~46*

To explore the mechanism of action of the four famous herbs produced in the Huai area, their decoction were administrated to mice through gastrogavage, then the activity of MAO in the brain chondriosome was determined. The results showed that in the Shan Yao and Niu Xi groups, the activity of MAO was lower than that of the control group ($P < 0.05$); in the mixture group, the activity of MAO was significantly lower than that of the control group ($P < 0.01$). This research indicated that the four famous herbs produced in the Huai area could lower the activity of MAO in the brain chondriosome in mice.

—Zeng Kai, et al. *The influence of the four famous herbs consisting of Shu Di, Ju Hua, Shan Yao and Niu xi produced in the Huai area over the activity of MAO in brain chondriosome of mice. Chinese journal of gerontics, 1998; 18(4): 102*

Contra-indications

Aside from the known contra-indications and interactions of Chinese herbs specific prohibitions are known for MAOI's. It is recommend that users avoid aged cheese; aged or cured meats (e.g., air-dried sausage); any potentially spoiled meat, poultry, or fish; broad (fava) bean pods; Vegemite / Marmite concentrated yeast extract; sauerkraut; soy sauce, soy products and soy bean condiments; and tap beer. Wine and domestic bottled or canned beer is considered safe when consumed in moderation. Other foods not mentioned are considered unrestricted.

Caution is urged when combining with SSRIs as Chinese herbs may potentiate the action depending on the type of depression or if anxiety is present.

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Observation on changes of urine 17-OHCS output in patients with Kidney-deficiency

In the late 1950's, *zang*-state Research Group of Shanghai No. 1 Medical College studied the differentiation and treating rules of Kidney-*yin* and Kidney *yang* with Integrated Traditional and Western Medicine methods. During the research, they found that in patients with Kidney-*yang* deficiency, 24 hours' 17-hydroxycorticosteroid (17-OHCS) was lower than that of normal individuals ($P < 0.01$); while the average value of urine 17-OHCS of patients with Kidney-*yin* deficiency was on the high side within the normal range or higher than normal value, but the values varied greatly among the individuals and had no statistical significance.

ACTH test was used in patients with Kidney-*yang* deficiency, half the cases had a delayed reaction, but the maximum value of the reaction could still reach the normal level; the other half cases had an approximate normal reaction.

According to the results, researchers believed that reversible metabolic disturbance of adrenal cortex may contribute to Kidney-deficiency of TCM.