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Dietary and botanical anxiolytics

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Summary

Drugs used to treat anxiety have many negative side effects including addiction, depression, suicide, seizures, sexual dysfunction, headaches and more. Anxiolytic medications do not restore normal levels of neurotransmitters but instead manipulate the brain chemistry. For example, selective serotonin reuptake inhibitors (SSRIs) prevent the reuptake of serotonin from the synapse allowing serotonin to remain in the area of activity for a longer period of time but does not correct the lack of serotonin production. Benzodiazepines, such as Valium and Xanax®, stimulate GABA receptors, thus mimicking the calming effects of GABA but again do not fix the lack of GABA production. Often, the brain becomes accustomed to these medications and they often lose their effectiveness, requiring higher doses or different drugs. In contrast to anxiolytic drugs, there are herbs and nutrients which can stimulates neurotransmitter synthesis and more naturally effect and even adjust brain chemistry in the absence of many of the side effects experienced with drugs. Therefore this paper explores several herbal and nutritional approaches to the treatment of anxiety.

key words: **anxiolytic • anxiety • Kava Kava • nutrition • botanical medicine**

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Background

Anxiety is a mood of fear, worry, and uneasiness resulting from the apprehension of something bad happening and has widespread deleterious social consequences. While anxiety can be a normal beneficial response to events that truly threaten ones security, chronic and irrational anxiety in response to normal life events in the absence of genuine threats can be debilitating and is considered to be an anxiety disorder. In developed countries, anxiety disorder rates range from 13.6% to 28.8% of the population. In the United States, anxiety disorders effect 40 million people above the age of 18 [1]. Further, in developed nations, women are between two and three times more likely to experience generalized anxiety disorder compared to men [1–6]. Anxiety can be the consequence of a variety of causes and arise in individuals through various different chemistries. For example, anxiety can be the consequence of dietary deficiency, hormonal changes, illness, traumatic experiences, bad habits, life stressors, aging, and genetics. In specific vitamin, mineral and amino acid deficiencies in the diet are associated with increased risk for anxiety disorder. Changes in hormonal balances, particularly associated with women during menstruation, pregnancy, post-partum periods, and menopause are all associated with increased frequencies of anxiety disorder. Further, a traumatic violent experience may lead to post-traumatic stress disorder in which a person will feel anxiety when the environment reminds them of the original violent experience. Bad habits can also lead to anxiety. For example, illicit drug abuse and even over consumption of caffeine or lifestyle choices can lead to anxiety. Hospitalization due to a diagnosis with a serious illness such as HIV/AIDS and cancer can increase the risk for anxiety. Moreover, often the stress and discomfort associate with the treatments that go along with these illnesses increase the risk for anxiety. With regard to an inherited genetic basis for anxiety, some studies suggest that variation in neurotransmitter receptor genes are associated with certain forms of anxiety. In addition anxiety often occurs in conjunction with other psychiatric or medical conditions, such as depression, chronic fatigue, cardiac disease, or respiratory compromise. Moreover, chronic anxiety is associated with greater risk of morbidity and mortality due to both cerebrovascular and cardiovascular diseases as well as a range of other neurological disorders [6–8]. Further, persons with anxiety disorders are at increased risk of suicidal behavior when faced with adverse life events such as divorce or financial difficulties [9]. Anxiety is also closely associated with other mental health conditions, especially depression. This relationship can work both ways causally. For example, anxiety can lead to depression and depression can lead to anxiety. In the National Co-morbidity Survey, the co-occurrence of anxiety and depression is in 58% of the cases. Interestingly, in this regard, anti-depressive medicines can be used to treat anxiety, even when there is no co-morbidity which is suggestive of common neurophysiologies and perhaps even common causes. Indeed the neurochemistry of anxiety and depression is similar, each sometimes involving imbalances of dopamine and serotonin making anxiety difficult to diagnose and treat effectively. In part, due to the overlapping chemistry and treatment between anxiety and depression, the use of diet, herbs and lifestyle changes is a valuable means both treat anxiety and depression and dissect the causes of anxiety from the causes of depression.

There are five main types of anxiety disorder. They are generalized anxiety disorder (GAD), panic disorder, obsessive compulsive disorder, phobia and post-traumatic stress disorder. In all cases, central nervous system neurotransmitter levels are inappropriate and/or the HPA axis is imbalanced. Generalized anxiety disorder (GAD) is characterized by worry in the absence of a real threat or problem. People with GAD are constantly apprehensive and are unable to relax. People with GAD experience insomnia and fail to concentrate well. A person with mild GAD can manage to keep a career and a social life, however, severe GAD can lead to failure at work and an avoidance of social situations. Women are at a greater risk for GAD than are men and a diagnosis of GAD is made when an individual three or more of the above symptoms almost daily for six consecutive months [10,11]. Panic disorder is sudden attacks of fear and a sense of impending doom. This can cause elevated heart rate, sweating, and dizziness. During a panic attack the person experience shortness of breath, nausea and chest pain. Often these physical symptoms can feedback and make the panic attack worse. Panic attacks are unpredictable and sudden and are roughly 10 minutes long. A person with panic disorder will avoid places where past attacks have taken place and even conditions similar to those places. Panic disorder often leads to lost jobs. Panic disorder effect 6.0 million Americans, and is twice as common in women as it is in men [1,12]. Obsessive-compulsive disorder (OCD) is characterized by persistent thoughts (obsessions). The obsessions then cause anxiety and this anxiety leads to the use of ritualistic actions (compulsions) in an attempt to alleviate this anxiety [13,14]. A good example of OCD is an obsession with bacteria in the environment and a subsequent compulsion wash hands repeatedly. Approximately 2.2 million American adults suffer with OCD and OCD affects men and women equally [1]. Phobias are unjustifiable fears. There are specific and social phobias. Specific phobias are a fear of certain objects while social phobia is anxiety about everyday social situations. Social phobia is a chronic fear of being judged by others. A social phobia can last weeks prior to a scheduled encounter or social event. Social phobias affect a 15 million Americans [1,15,16]. Posttraumatic stress disorder (PTSD) is initiated through an experience of a traumatic or violent event. This could include a serious accident, a violent crime, or a natural disaster. People with PTSD relive this violent experience in nightmares or wakeful memories. Subsequent ordinary events can trigger "flashbacks" that cause the afflicted person to believe the event is happening again. Approximately 5.2 million Americans are affected by PTSD [1,17].

Screening tests for anxiety disorders are available to help determine the cause and severity of anxiety, however despite these tests, the diagnosis of anxiety disorders is partially subjective and based mostly on observation [18]. Once an anxiety disorder is diagnosed the treatments will usually involve several approaches that may including diet and lifestyle changes, relaxation and massage therapy, psychotherapy, behavioral therapy or cognitive-behavioral therapy, and drug intervention. Most recently Yoga and music have been used to treat anxiety disorder with some success. Cognitive-behavioral therapy requires the patient to consciously modification their thinking patterns regarding their own perceptions and sensations accompanying anxiety and fear. This form of therapy involves helping the patient to

recognize cognitive distortions, or and inaccurate perceptions of everyday issues. Patients are then taught how their own distortions produce their anxiety and panic, and the patient learns to recognize when their thinking is distorted and taught methods to cognitively replace the distorted thoughts with more accurate ones. Cognitive-behavioral therapy is an effective first-line treatment for all forms of anxiety [19,20]. Behavior therapy uses several techniques to teach the patient how to modify their behavior which can contribute to the feelings of anxiety. For example, breathing exercises teaches people how to control the physical signs of anxiety by taking slow, deep breaths, which helps control hyperventilation. Further, exposure therapy relies on small and progressive exposures to whatever frightens them the patient such that the gradual, and safe exposures reveal to the patient that the cause of the anxiety is really not that threatening.

The neurochemistry of anxiety disorders can be distilled into two main categories. First, is an imbalance in neurotransmitter (GABA, serotonin and dopamine) function in the amygdale; an area of the brain involved with the perception and assessment of threats. Second is the hypothalamic-pituitary-adrenal axis (HPA-axis) which involves brain stimulation of the adrenal gland to release cortisol, DHEA, adrenaline and noradrenaline. Cortisol is the stress hormone and adrenaline and noradrenaline increase heart rate and breathing in what is known as the "fight or flight" response.

Anxiety disorders are treated with anxiolytic medicines that fall into four categories. First, are the benzodiazepams that include xanax (alprazolam), klonapin (clonazepam), valium (diazepam) and ativan (lorazepam). These work by acting on the receptor for the neurotransmitter, GABA. Second, are the anti-depression drugs, which increase serotonin and dopamine levels and are the selective serotonin reuptake inhibitors (SSRI's) (Prozac, Zoloft, Paxil, Lexapro, and Celexa) and monoamine oxigenase inhibitors (MAOIs) (Nardil,Parnate, Marplan and Emsam) and tricylic antidepressants (TCAs). Third, are tranquilizers such as buspirone (BuSpar) which elevate serotonin and dopamine. Fourth are beta-blockers (blood pressure medications) which act on the HPA axis by blocking the effects of norepinephrine. In addition to being expensive, these medications, as mentioned above, can have harsh side effects such as, addiction, suicide, hallucinations, insomnia, headaches, loss of motor coordination, and can disrupt everyday activities such as driving, work and socializing.

Drug therapy targets two main circuitries in the body. The first is the amygdala and the second is the HPA axis. Recently, the HPA axis has been targeted for the treatment of anxiety using beta blockers which can affect the activity of norepinephrine, and cortisol (the stress hormone). The classic and well know anxiolytic medications target the activity of the neurotransmitters dopamine, serotonin, GABA. For example, benzodiazepines act by extending the life of gamma-aminobutyric acid (GABA), an inhibitory brain neurotransmitter within the synapses [21]. GABA is essential to limiting the excitation of neurons so that input signals are balanced and not overdone. Benzodiazepines relieve anxiety symptoms quickly. However, these drugs can become habit forming, and also, patients can develop a tolerance to them, which results in an increasing required dosage during treatment. After the use of benzodiazipenes, some individuals experience a variety of withdrawal symptoms which include seizures, confusion, memory loss, hyper-anxiety, and re-emergence of the original symptoms [22]. Commonly prescribed benzodiazepines include Valium® (diazepam), Xanax® (alprazolam), Klonopin® (clonazepam), and Ativan® (lorazapam). Tranquelizers such as azipirones are also anxiolytic medications that do not have the same tolerance and dependency issues as the benzodiazepines. These drugs are partial serotonin receptor agonists (promote receptor activity). BuSpar® (buspirone) is a member of the azipirone class prescribed to treat general anxiety disorder. Side effects include nausea, headaches, and dizziness. Antidepressant drugs can also be effective for treating anxiety, especially when the anxiety occurs in conjunction with depression. These drugs include the selective serotonin reuptake inhibitors (SSRIs) which increases the level of serotonin activity in the synapse and the less commonly used tricyclic antidepressants and monoamine oxidase inhibitors. These drugs are known to have potentially significant side effects. In 2004 the US Food and Drug Administration announced that the SSRIs must carry a strong warning advising patients of the increased risk of suicide among adolescents using these drugs. Popular SSRIs include Prozac® (fluoxetine), Zoloft® (sertraline), Luvox® (fluvoxamine), Paxil® (paroxetine), and Celexa® (citalopram). Recently, Beta-blockers include Inderal® (propranolol) and Tenormin® (atenolol) and are used primarily to treat heart conditions. However these drugs reduce heart palpitations and other physical HPA-related symptoms of anxiety and by controlling these feedback signals, the beta blockers offer a relatively new approach to treating some forms of anxiety. Potential side effects include sexual dysfunction, slow pulse, drowsiness, fatigue, dry mouth, numbness or tingling of fingers or toes, dizziness, diarrhea, nausea, weakness, and cold hands and feet [23].

In contrast to medicines, a number of nutrients and herbs have been identified which reduce anxiety by re-establishing a healthy diet and by altering both neurotransmitter levels and the HPA axis in the absence of the severe side effects. For example, vitamins C, D, and E, omega-3 fatty acids, and the green tea amino acid L-theanine are dietary supplements known to increase the production of dopamine. Further, supplementation with the amino acid L-tryptophan and its precursor, 5-HTP, and the B vitamins, vitamin D, selenium, and omega-3 fats increases serotonin production. These amino acid supplements are neurotransmitter building blocks and the vitamins act as cofactors in neurotransmitter biosynthesis pathways. This dietary approach can correct the underlying neurochemistry, unlike many of the drugs mentioned above which simply mask the problem.

Nutritional Approaches for Anxiety

Amino acids

The amino acid glutamate is the principle excitatory neurotransmitter and also used to make the neurotransmitter gamma-aminobutyric (GABA). L-tryptophan and L-tyrosine are precursors for the neurotransmitters, serotonin, dopamine, and norepinephrine. The ability of the body to produce these neurotransmitters is directly linked to the levels of these amino acids consumed in the diet [24].

L-tryptophan, L-tyrosine and L-phenylalanine

Dietary deficiency in L-tryptophan, L-phenylalanine, or L-tyrosine leads to low serotonin synthesis due to the lack of availability of these building blocks and this dietary deficiency is associated with anxiety [25–28]. Dietary supplementation with increased L-tryptophan is known to increases serotonin synthesis in rats and humans [25,26,29] verifying a nutritional approach to the treatment of anxiety. 5-hydroxytryptophan (5-HTP), the tryptophan precursor, elevates the levels of serotonin synhtesized in humans [30,31] and 5-HTP and tryptophan elevate brain serotonin levels are known to enhance a sense of well being [30–35]. Lastly, the increase in nutritional D,L-phenylalanine and L-tyrosine is known to increases synthesis of dopamine and norepinephrine [36] further supporting the role of nutrition in fighting anxiety.

L-lysine and L-arginine

Interestingly, L-lysine deficiency is known to increase the risk of anxiety in humans [37,38]. In clinical trials, supplementation of the diet with the amino acid nutrient arginine reduces synthesis of the stress hormone, cortical, in humans and may in this way be involved in the health of HPA-axis [39].

Minerals

Magnesium

In a placebo controlled clinical study, when magnesium was taken orally along with calcium supplements, anxiety in human subjects was decreased compared to placebo [40]. Similarly, supplementation with magnesium and vitamin B_6 was shown to reduces premenstrual-related anxiety and GAD in women [41,42]. Animal research supports this observation with a mouse-model of magnesium deficiency that leads to anxiety behavior in mazes. Most interesting is that the anxiety in these mice is reversed with diazepam treatment, and with magnesium supplementation supporting the observation that nutrients can perform as well as anxiolytic drugs [43].

Selenium

In clinical trials people given daily oral supplementations of 100 mg of the nutrient, selenium, for 5 weeks reported less anxiety [44–46]. Further, selenium added to the diet also reduced the anxiety in hospitalized patients who are elderly, cancer patients, and/or HIV patients [47–49].

Fatty acids

Omega-3 fatty acids

Dietary omega-3 fatty acids has been shown to both improve mood and reduced the risk of anxiety [50–52]. In one clinical study, students studying for exams were given 2.5 g/day of omega-3 (n-3) polyunsaturated fatty acids and the students receiving these supplements had a 20% reduced rate of in anxiety [53]. In a three month clinical study, omega-3 fatty acid supplementation reduced anxiety in patients who had been substance abusers suggesting a role for nutrition in managing hospital and withdrawal related anxiety [54].

Vitamins

Vitamin C is a cofactor for enzymes involved in biosynthesis and supplementation with this vitamin reduces anxiety by limiting the oxidative stress from metabolites and also by limiting cortisol [55]. One clinical study with humans showed that high dose vitamin C improves mood [56]. Vitamin E also reduces anxiety in humans [57] and vitamin D reduces anxiety in people with fibromyalgia-associated anxiety [58,59].

Herbs and Botanical Medicine for Anxiety

In addition to nutrients such as amino acids, minerals and vitamins, dietary supplementation with herbs and plant products have also been shown to be effective in treating anxiety [60–64]. These herbs are not neurotransmitter building blocks or enzyme enhancers, but may have less harsh effects when compared to anxiolytic medicines.

St. John's wort (Hypericum perforatum)

St. John's wort is an aromatic perennial plant that is native to Europe and parts of Asia, North America, and South America and has been widely used as an anti-depressant. In fact the majority of clinical studies that compare it with antidepressant drugs found it superior to the placebo [65–67]. St. John's wort increases brain levels of serotonin [68,69] and also normalizes the HPA-axis by reducing inflammatory and oxidative stress [61]. Recently, two clinical studies show that dietary supplementation with St. John's wort can reduce anxiety in women associated with premenstrual syndrome (PMS) [70,71]. However, St. John's wort is should not be used during pregnancy, lactation, and exposure to strong sunlight and should not be taken along with antidepressant medication [72].

Ginkgo biloba

Animals given nutritional supplements of Ginkgo biloba demonstrated reduced anxiety [73,74]. Further in controlled clinical studies using MRI, Ginkgo biloba extracts were shown to activate GABA pathways and act like a benzodiazepine and reduce anxiety in patients with GAD [75,76].

Ashwagandha (Withania somnifera)

Ashwagandha, an herb with anti-inflammatory and rejuvenating qualities [77]. Rodents treated with ashwagandha showed reduced anxiety behavior compared to control treatment. This reduction matched the reduction in anxiety in these rodents when treated with several benzodiazepine drugs [78–80], again supporting the concept than anutritional herbal supplement can act to replace the need for harsh drugs. In addition to rodents, Ashwagandha has also been shown in clinical studies to reduce anxiety in patients which were divided into two groups and were either provided psychotherapy or treated with ashwagandha [81–83]. In this case, the ashwagandha treated group demonstrated a greater reduction in anxiety parameters compared to those receiving psychotherapy [84].

Kava kava

Kava is a preparation from the plant *Piper methysticum* which contains six psychoactive kavalactones that bind to GABA

receptors, dopamine receptors and opiate receptors and work to uncouple the sodium potassium channels thereby reducing impulses to muscles and serves as a muscle relaxant [60]. Of all of the anxiolytic herbs, Kava is the most studied and also demonstrates the best results against mild anxiety and anxiety disorders in humans [85–87]. In 1997, anxiety patients were given the kava extract for 25 weeks and compared to the placebo these patients had significantly reduced anxiety [88]. Subsequent clinical studies confirm that dietary kava is an effective treatment and benzodiezepam replacement and treatment for anxiety and PMS [89–93].

Valerian (Valeriana officiaonalis)

Valerian is a temperate root and has been since the time of Hippocrates. Valerian root components have been shown to both increase GABA synthesis and decrease synaptic GABA reuptake [94]. Valerian root activates glutamic acid decarboxylase, an enzyme involved in the synthesis of GABA [95]. The active Valerian root extract known as valernic acid acts as a GABA agonist by binding to GABA receptors in cell culture systems [96–98]. These Valerian root extracts have anxiolytic properties for rodents [99–101] and in people when taken at doses of 400–900 mg daily valerian root was as effective as diazepam in the in reducing anxiety in psychiatric rating scales [102–105]. Again, these studies show that dietary supplementation can be as effective as drugs in reducing anxiety.

GABA

GABA is a neurotransmitter and is found occurring naturally in herbs and plants. GABA is the main inhibitory neurotransmitter and works by reducing the excitability of a neural network thereby functioning as a brake on the neural circuitry during stress. Indeed, low GABA levels are associated with, restlessness, anxiety, insomnia and a poor mood state [106–108]. Dietary GABA supplement in clinical studies relieves anxiety and increases alpha brain waves, which are associated with relaxation [109–111].

Theanine

Theanine is an amino acid found in green tea. Theanine produces a calming effect on the brain [60,112,113]. Theanine crosses the blood-brain barrier and increased the production of both GABA and dopamine [114,115]. In a clinical study, healthy volunteers were given theanine and a benzodiazepine and subjected to experimentally induced anxiety. The people who received theanine had lower baseline anxiety throughout the trial [116].

Hops, Lemon Balm, Skullcap, Passionflower, Rosenroot and Chamomile

Extracts from skullcap (genus *Scutellaria*), hops (*Humulus lupulus*), dried passion flower (genus *Passiflora*), Chamomile (*Matricaria recutita*), and lemon balm (*Melissa officinalis*) are also all reported to reduce anxiety [105,117–123]. Lemon balm increases synaptic GABA and reduced cortisol in animals [60]. Skullcap components, bacalin and bacalein, are GABA receptor agonists and promote GABA activity [60;95]. Magnolia and Phellondendron bark have beneficial anxiolytic effects in premenopausal women [124]. A clinical study showed that dietary supplementation with 340 mg of a Rosenroot for 10 weeks reduces generalized anxiety disorder [125].

Anxiety and Hormones

Anxiety disorders in general affect more women than men. Further, pregnant, postpartum, premenstrual and menopausal women also experience symptoms of anxiety to a greater extent than at other times in life. This general observation has lead scientists to investigate a hormone-anxiety link. By now, it is well known that most steroid hormones (e.g., pregnenolone, estrogen, progesterone, testosterone, and DHEA) are neurologically active. In fact, large quantities of DHEA, as well as estrogen and progesterone receptors, are found in the brain. These hormones have a number of effects within the brain, including regulation of mood. Accordingly, a number of studies have linked abnormalities in hormone levels to various anxiety disorders [126–129]. Further, in the first week of menses with increases in estrogen, women produce more serotonin and have improved mood and decreased estrogen and serotonin is associated with the premenstrual period [130]. Further, the drop in estrogen during menopause is associated with reduced serotonin production. In this regard, the selective serotonin reuptake inhibitors (SSRIs) used to treat anxiety have also been shown to improve mood and cognitive function in menopausal women [131].

It is also important to examine the relationship between the stress hormone cortisol and DHEA (the metabolite building block for the sex the steroid hormones) During times of prolonged stress a greater proportion of cortisol is made compared to DHEA such that increased blood cortisol/DHEA ratios are a marker of stress and dysfunctions that lead to this state are associated with anxiety disorder [132]. In an animal study that compared normal mice to mice that lacked a progesterone receptor, researchers found that progesterone decreased anxiety behavior through a mechanism of action similar to that of benzodiazepines by acting on GABA receptors [133]. Another study found that a single dose of progesterone given to animals decreased anxiety indicators during stress tests, while the abrupt cessation of progesterone therapy increased measures of anxiety [134]. Clinical studies with DHEA supplementation has been found to be particularly helpful in relieving anxiety in females with low hormone levels [135].

Researchers have found in double blind randomized placebo controlled clinical trials, that St. John's wort reduces the duration and severity of hot flashes in both premenstrual and premenopausal women [145]. In addition, the Central American plant, Piper hispidum Swingle, has been traditionally used to treat dysmenorhea and pain in Guatemala and contains molecules that bind to both the estrogen receptor and serotonin receptors in human cells [136]. Extracts of the Chinese herb, Fructus Sophorae has also been shown to ease anxiety in menopausal women [137] and reduced anxiety in postmenopausal women has been achieved in placebo controlled studies by supplementing with 80 mg/day for 90 days of red clover isoflavinones [138]. Vitex agnus-castus (chaste tree/berry) when taken over a 16 week period in combination with St. John's wort also reduced anxiety associated with premenstrual syndrome and menopause [71]. A

metabolite of the isoflavone daidzein from soy has also been shown to reduce anxiety in premenopausal, perimenopausal and postmenopausal women [139,140]. Lastly, in healthy cycling women of reproductive age, a preparation combining magnolia and Philondendron bark has been shown to reduce anxiety for women [124]. Nutritional supplements including calcium, vitamin D3, lycopene, bioflavoids and even the probiotic lactobacilli have been shown in various combinations to reduce anxiety symptoms including panic disorder associated with menopause [27,141]. Post-partum associated anxiety is significantly reduced in some cases with 100 mg/day selenium supplementation [46].

In addition to herbal and nutritional approaches to control and regulate the effects of decreasing estrogen on serotonin levels and anxiety, it is also important to examine the relationship between the stress hormone cortisol and DHEA (the metabolite building block for the sex the steroid hormones) During times of prolonged stress a greater proportion of cortisol is made compared to DHEA such that increased blood cortisol/DHEA ratios are a marker of stress and dysfunctions that lead to this state are associated with anxiety disorder [132]. In an animal study that compared normal mice to mice that lacked a progesterone receptor, researchers found that progesterone decreased anxiety behavior through a mechanism of action similar to that of benzodiazepines by acting on GABA receptors [133]. Another study found that a single dose of progesterone given to animals decreased anxiety indicators during stress tests, while the abrupt cessation of progesterone therapy increased measures of anxiety [134]. Clinical studies with DHEA supplementation has been found to be particularly helpful in relieving anxiety in females with low hormone levels [135].

Conclusions

Anxiety is a generalized mood of fear, worry and or uneasiness that results from an bad felling about something that happens or may happened. It can be stimulated from environment factors, or result from bad habits or social situations. There are different types of anxiety that could be mild or sever depending on the level of the disorders. Anxiety, as with other medical problems, can be diagnosed and treated by different therapies, such as cognitive-behavioral therapy, panic disorder, and drug therapy. Using drugs is a common but harsh way to treat anxiety disorders. However more natural treatments including amino acid, minerals, and fatty acids can reduce anxiety. Further, herbs and botanical medicine, such as St. John's wort (*Hypericum perforatum*), Ginkgo biloba, Kava Kava, which have different roles to reduce many psychiatric disorders, also reduce anxiety. In this regard, anxiety may be managed without the harsh side effects of pharmaceuticals using nutritional and botanical treatment as well as life-style changes.

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