

## PSYCHOPHARMACOLOGY

### The Use of Kava and Cognitive-Behavior Therapy in the Treatment of Panic Disorder

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*This article proposes the use of the herb kava in combination with cognitive-behavior therapy (CBT) in the treatment of panic disorder in lieu of traditional psychopharmacologic agents such as benzodiazepines and antidepressants. The properties of kava are discussed, as well as their therapeutic effects with anxiety. A single, non-placebo-controlled case example is described, along with 6-months follow-up treatment effects combined with CBT. The potential pitfalls of using the herb are addressed, particularly the combination of kava with psychopharmacologic compounds.*

IT IS QUITE CLEAR, without conducting an exhaustive review of the professional literature, that the treatment of choice for panic disorder involves the use of a combination of interventions (Cottraux et al., 1995; Klosko, Barlow, Tassinari, & Cerny, 1990). In fact, the most recent practice guidelines for the treatment of panic disorder, as set forth by the American Psychiatric Association (APA; 1998), for the first time underscored the notion of using a combined treatment approach. Therapeutic options presented include psychiatric management, pharmacological interventions, and psychosocial treatment. This package also contains a psychoeducational component that has been found to be effective in defusing the mystique surrounding panic (Barlow & Lehman, 1996).

Pharmacotherapy, particularly the use of tricyclic antidepressants and benzodiazepines, has been the medical treatment of choice in most settings involving acute anxiety or panic (Barlow, Gorman, Shear, & Woods, 2000; Liebowitz, Fryer, & Gorman, 1986; Noyes et al., 1984). This is particularly so with the benzodiazepines as they are fast acting and effective medications for blocking panic (Ballengier et al., 1988). High-potency benzodiazepines are also the most frequently distributed by physicians and hospital emergency rooms for patients complaining of panic attacks (McNally, 1994). Studies involving the combined use of cognitive-behavioral treatment (CBT) and benzodiazepines show that CBT can be at least equally as effective as pharmacotherapy in terms of pretreatment severity and acute treatment outcome (Barlow et al., 2000; Otto, Pollack, & Maki, 2000; Pollack, Otto, Kaspi, Hamerness, & Rosenbaum, 1994). Data also indicate that initiating benzodiazepines and CBT is typically help-

ful, and initiating benzodiazepines and later adding CBT is also effective; however, adding benzodiazepines subsequent to the start of CBT shows poor results (Otto, Gould, & McLean, 1996).

There has also been mention in the past of using monoamine-oxidase inhibitors (MAOIs; Sheehan, Ballengier, & Jacobson, 1980) and, more recently, the emergence of the selective serotonin reuptake inhibitors (SSRIs; Barlow et al., 2000). New synthetic drugs that are currently being assessed for the treatment of anxiety are 5-hydroxytryptamine receptor agonists and the substance P inhibitor MK-869 (Bonn & Bonn, 1998).

While these compounds remain the treatment of choice, clinicians know all too well that there are many individuals who do not tolerate certain pharmacological agents, either because of difficulties with metabolism, conditions of pregnancy and/or lactation, or the mere fact that some patients simply do not care to use medication. Dropout rates of 15% to 28% have been reported in the literature for individuals using medication (Craske, 1996). In addition, certain compounds, particularly benzodiazepines, are not without untoward side effects, especially if they are used for an extended period of time (Rachman, 1990). Serious side effects include dependence, sedation, and memory impairment (Priest & Montgomery, 1988). The tendency toward relapse rates are also as high as 50% or more (Marks et al., 1993; Spiegel, Bruce, Gregg, & Nuzzarello, 1994).

As an alternative to medication, the use of the herb kava is proposed in the treatment of panic disorder, especially when combined with psychotherapy, such as CBT. Natural or "alternative" remedies, derived from natural products but not approved by the U.S. Food and Drug Administration (FDA) for their putative indications, have been used for centuries (Schulz, Hänsel, & Tyler, 1998). They have recently gained increasing attention in the treatment of anxiety. Recent data suggest that individuals who suffer from anxiety frequently use alternative therapies (Astin, 1998).

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 **Continuing Education Quiz located on p. 167.**

Kava has been used extensively in the treatment of generalized anxiety disorders (Connor & Vaughan, 1999). Although kava has been known for centuries, Western cultures have only become familiar with it as a result of the request for alternative remedies (Flanagan & Jurens, 2000). The kava root (known scientifically as *Piper methysticum*) was first introduced to the West by Captain James Cook during his voyage to the South Seas in 1768. The actual origin of kava remains unknown, but it has been used by the oceanic people of the Pacific Islands—Micronesia, Melanesia, and Polynesia—for centuries. Kava, often used to induce a sense of tranquility and enhance sociability, has had an integral role in a variety of social and therapeutic settings. Only recently has its calmmative properties gained broader, worldwide recognition (Connor & Vaughan, 1999; Pittler & Ernst, 2000).

The kava plant is a perennial shrub belonging to the Piperaceae family. The plant is indigenous to Oceania and is used widely in the South Pacific for its intoxicating effects. Kava is marketed as a mild anxiolytic in European countries. In the United States, kava is sold in health food stores without a prescription as a natural alternative to anxiolytic and hypnotic agents.

The active component of kava belongs to a group known as alpha-pyrone and is present in the root extract. Pharmacologic studies indicate additive effects between kava alpha-pyrone, phenobarbital, and pregnane steroids. On the other hand, these investigational studies suggest that kava might produce addictive effects with benzodiazepines, given that they act on the same receptor sites and on the same areas of the central nervous system with increased gamma-aminobutyric acid (GABA) receptors (Jussofie, Schmitz, & Hiemke, 1994).

Other studies suggest that individuals may develop clinical signs suggestive of central dopaminergic antagonism after exposure to various kava preparations (Schelesky, Raffauf, Jendroska, & Poewe, 1995).

It is believed that the pharmacological action of kava is due primarily to kavalactones or kava alpha-pyrone, which are found in the fat-soluble portion of the root. Kava extracts have been shown to exert scientific benefit with regard to anxiety and possess no addictive potential (Connor & Vaughan, 1999). In addition, kava has sedative, analgesic, mild anticonvulsant, and muscle relaxant effects. It is the anxiolytic properties, however, which have been most widely investigated in European studies. Neurochemically, kava is believed to bind to receptor sites in the brain, especially in the amygdala (Y. N. Singh, 1992). Its particular influence on GABA is still not totally clear, although it is hypothesized to work in a similar fashion as benzodiazepines (Jussofie et al., 1994).

In one double-blind study, 58 subjects with generalized anxiety disorders were randomly assigned to treatment with either kava, 100 mg (equivalent to 70 mg kava-

lactones [kl]), or placebo 3 times a day for 4 weeks. The kava group demonstrated significant reduction in anxiety compared to the placebo group, as measured by changes on the Hamilton Anxiety Rating Scale (Kinzler, Krömer, & Lehmann, 1991). Furthermore, Volz and Kieser (1997) studied 101 outpatients with anxiety disorder. Subjects received randomly allocated, double-blind treatment with either kava, 300 mg (equivalent to 210 mg kl), or placebo daily for 25 weeks. By the 8th week of treatment, significant reductions were observed on the Hamilton Anxiety Rating Scale in the kava group, and these differences persisted throughout the entire clinical trial period. Woelk (1993) conducted a 6-week control trial comparing kava (210 mg kl/day) with oxazepam (15 mg/day) or bromazepam (9 mg/day), with no significant differences reported. One hundred and sixty-four subjects completed the clinical trial, suggesting that the effects of kava were comparable to benzodiazepines in this specific sample.

More recently, a systematic review and meta-analysis was conducted by Pittler and Ernst (2000). Double-blind, randomized, placebo-controlled trials of oral kava extract for the treatment of anxiety were included in the study. Superiority of kava extract over placebo was suggested by all seven reviewed trials. The meta-analysis of three trials suggests a significant difference in the reduction of the total score on the Hamilton Anxiety Rating Scale in favor of kava extract. These data imply that kava extract is superior to placebo as a symptomatic treatment for anxiety.

Unfortunately, very few controlled studies have been conducted in the United States using kava. One reported trial has assessed the effect of kava (240 mg kl per day) versus placebo on daily stress and anxiety in 160 nonclinical participants. Subsequent to 4 weeks of treatment, a significant reduction in the stress and anxiety associated with life's daily hassles was noted only in those receiving kava (N. Singh, Ellis, & Singh, 1998). Currently, a randomized, double-blind placebo-controlled trial of kava on generalized anxiety disorder subjects is under way (Conner, 1999). To date, no preliminary data have been reported, particularly in the treatment of panic.

In addition to the shortage of clinical studies on the effects of kava with anxiety disorders, there is also an absence of studies observing the effects of kava on panic disorder. No studies to date have observed its potential effects. Even the Volz and Kieser (1997) study, which used a heterogeneous group of subjects with anxiety disorders, failed to include subjects that were diagnosed with panic disorder. It is hypothesized that if kava can be effective with other types of anxiety disorders, it may have potential effectiveness with panic disordered individuals as well. The following description is an example in which kava was used in a single, noncontrolled case study for the treatment of panic disorder.

### Case Example

Maggie<sup>1</sup> was a 38-year-old, white, separated female at the time that she presented for treatment with complaints of panic attacks. She initially reported symptoms that included increased heart rate, pressure or heavy feelings in the chest, dyspnea, nausea, and experiencing a lump in her throat. Maggie reported experiencing these symptoms abruptly one day shortly after her husband served her with notice that he was filing for divorce. This notice came after several years of chronic marital problems deemed by Maggie's husband to be irreconcilable. Maggie's first panic attack occurred while she was driving home from work one evening in the car on the highway. She experienced additional panic attacks at work and also several at home throughout the subsequent weeks, totaling approximately five to six attacks per day. Maggie reported fearing the effects of these symptoms as well as negatively anticipating subsequent attacks. She reported that, often, her fear of having attacks was actually enough to generate the symptoms alone. Maggie also qualified for an adjustment disorder with anxiety on Axis I (with no diagnosis on Axis II or III). These panic symptoms included the same symptoms mentioned above, with additional sensations of lightheadedness and dizziness as the initial symptoms worsened. After 2 weeks of experiencing panic attacks, Maggie consulted with her naturopathically oriented physician, who, instead of prescribing her medication, referred her to a clinical psychologist for "non-drug treatment." It was both the physician's intention as well as Maggie's aim to try to avoid the use of any psychotropic medication.

Upon discussing some of the treatment options, Maggie expressed her interest in non-drug treatments and appeared to be receptive to the notion of cognitive-behavioral interventions. It was a recommendation, however, to combine her therapy with the use of kava, a natural herb—something that was acceptable to her. This was decided after Maggie expressed her need to have something to reduce her panic attacks more immediately until the treating psychologist had returned from a 2-week vacation. Since the scheduled vacation would delay treatment, it was a viable alternative to exercise a trial of kava under the direct medical supervision of her family physician.

Maggie was initially started on a dose of kava of 280 mg per day consumed as two capsules or gel caps. This was standardized at 30%<sup>2</sup>. The amount was divided in stan-

dard doses 3 times per day and initiated during the first treatment session. The initial dose was conducted in conjunction with her family physician and was monitored by him on a regular basis. This was subsequent to a full physical exam that included a complete blood profile with platelet studies, an electrocardiogram, and an electroencephalogram, all of which yielded normal results.

Maggie was initially assessed with the Anxiety Disorders Interview Schedule–IV as well as the Body Sensations Questionnaire and the Beck Depression Inventory–II (BDI-II). The BDI-II was used specifically to monitor her level of depression before and after treatment. The following includes a full description of each of these measures.

### Assessment

*The Anxiety Disorders Interview Schedule–IV (ADIS-IV).* The ADIS-IV (DiNardo, Brown, & Barlow, 1995) is a structured interview process designed to assess comprehensively the DSM-IV anxiety and mood disorders. It also evaluates the presence of coexisting disorders and aids the clinician in rendering a differential diagnosis between panic disorder and other anxiety disorders. In addition, it evaluates symptom severity, degree of impairment, and clinical history. The ADIS-IV is widely used by clinicians and in research facilities treating panic.

*Body Sensations Questionnaire (BSQ).* The BSQ is an 18-item instrument designed to measure body sensations associated with panic and agoraphobia (Chambless, Caputo, Bright, & Gallagher, 1984). The specific items were generated from interviews from clients and therapists in an agoraphobia treatment program. The BSQ contains items that clients report to be disturbing that are associated with anxiety. The BSQ has very good internal consistency, with an alpha of .87. It also has good stability, with 1-month test-retest correlations of .67, and good concurrent validity, correlating with other measures of psychopathology. The BSQ is scored by summing the individual item ratings and by dividing the number of items rated. The mean score is 3.05 with a standard deviation of .86.

*Beck Depression Inventory–II (BDI-II).* The BDI is a 21-item, self-report instrument designed to assess the affective cognitive physiological and motivational features of depression in terms of both presence and severity (Beck, Steer, & Brown, 1996). Each item is rated on a 4-point scale (0 to 3) yielding a summary score that ranges from 0 to 63. The higher the score, the more severe the depression.

The BDI-II has demonstrated high internal consistency, with alpha coefficients ranging from .91 to .93 (Beck et al., 1996; Dozios, Dobson, & Ahnberg, 1998). Also, adequate content validity and factorial validity has been recorded.

Maggie met DSM-IV criteria for panic disorder, experiencing between four to seven full panic attacks within 3

<sup>1</sup>The name and basic background information have been changed in order to protect the identity of the patient in this case.

<sup>2</sup>The standardization of kava is essential because standardization signifies that the kava contains specific concentrations of the herb's active ingredients in every dosage unit and thus has consistency of therapeutic effect. In standardized doses, the kava should contain kavalactones of 30% or more.

days. Her results on the ADIS-IV indicated that she met the full criteria for panic disorder, particularly because her fear of experiencing subsequent panic attacks was sufficient to generate panic symptoms and that they often occurred "out of the blue," with a rapid rate of escalation. Baseline data were collected over a 3-week period between the initial assessment period and the actual start of treatment (see Figure 1). She was educated on the dynamics of anxiety and panic as well as how kava would be used in concert with cognitive-behavior therapy (CBT). Subsequent to the psychoeducational component, Maggie was also introduced to the panic diary, which was designed to help her keep track of her daily panic attacks during the interim between treatment sessions (Dattilio & Salas-Auvert, 2000).

Maggie was taught progressive muscle relaxation and breathing retraining via controlled breathing and received a self-instructional audiotape to help her carry out the exercises. She was also taught how to reinterpret interoceptive body cues via the use of the SAEB system—a conceptualization measure and restructuring guideline designed by the author (Dattilio, 1990, 1994).

This conceptualization system was designed to help individuals see how their cognitions and behaviors interfere with the exacerbation of their anxiety symptoms. It was also designed to provide them with some measure for restructuring automatic thoughts and reducing behaviors that contribute to the escalation of autonomic symptoms. Interoceptive cues triggering specific focus was placed on the dyspnea, increased heart rate, and pressure or heavy feelings in the chest.

## Results

Figure 1 illustrates the results of the combined scores on the BDI and the BSQ. It is clear to see that there was a significant reduction in panic attacks within 2 weeks of the onset of the use of kava. Maggie reported a continued reduction in panic as she proceeded through the treatment mode utilizing cognitive-behavioral techniques. This was reported in her panic diary as well as in her weekly verbal reports to her therapist. The kava was titrated gradually over the course of a 3-week period (see Figure 1).

Due to the severity of Maggie's panic symptoms, the results indicate that kava was effective in combination with CBT in helping Maggie to reduce the intensity of her panic. It was also effective in helping her to benefit more expediently from the use of CBT. She continued to be monitored medically by her family physician, who conducted an examination of her vital signs, periodic blood studies, and an electrocardiogram. In addition, a liver function screening yielded normal results. A 6-month follow-up period indicated no relapse of panic symptoms.

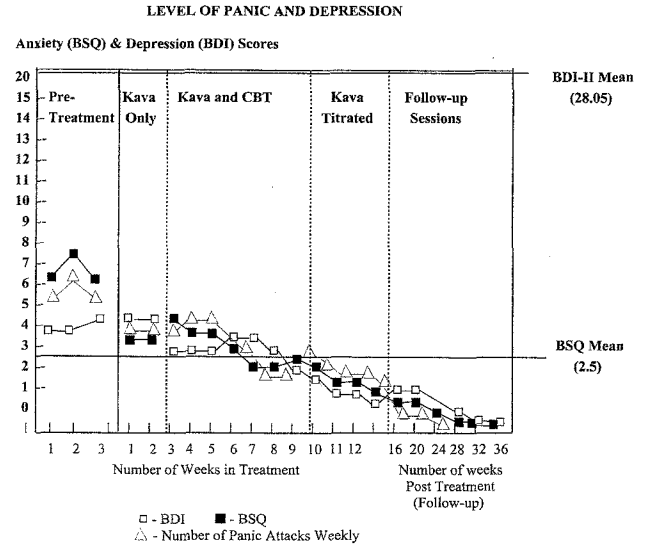


Figure 1. Level of panic and depression.

The use of kava was titrated gradually over a 3-week period (see Figure 1), with no reported withdrawal effects. The titration schedule involved a 20% reduction of the herb over the course of the 3 weeks.

## Discussion

There are a number of caveats in interpreting the data obtained from this single, non-placebo-controlled case. For one, regression to the mean may be a partial explanation for why symptoms of panic began to abate after the administration of kava. Thus, the generalizability is threatened unless the case study were to be repeated using a higher number of subjects and an adequate control. The results may be further confounded by the fact that the known variability of panic disorder and the limited data make it difficult to infer if change was due to the natural course of the disorder, kava, CBT, or the combined interaction. In addition, Maggie also qualified for a diagnosis of adjustment disorder with anxiety on Axis I, which may have accounted in part for the reduction of her symptoms with the mere passage of time.

This initial case experiment, however, does suggest that further research on the use of kava for the treatment of panic disorder may be worth investigating. The National Institutes of Health and the National Institute of Mental Health have recently acknowledged the importance of answering such questions and have begun to support more rigorous, placebo-controlled trials (Mischoulon & Rosenbaum, 1999).

Kava appears to be a safe and potentially effective component for augmenting the short-term treatment of anxiety disorder and may be a potential alternative to the use

of benzodiazepines and other compounds when treating panic, particularly in that it has demonstrated some success with other types of anxiety disorders (Connor & Vaughan, 1999).

Clinical and research experience reveal that recommended doses of kava are often well tolerated by patients. Side effects are uncommon, but they may include mild gastrointestinal discomfort, headache, dizziness, photosensitivity, and allergic skin reactions (Hofmann & Winter, 1996; Siegers, Harold, Krall, Meng, & Habs, 1992). In the aforementioned case, Maggie did not manifest any of the reported side effects, even with a dose as high as 280 mg per day. There was also no indication of any subtle visual impairment that is typically observed with high doses of kava. It should also be kept in mind that the potential for drug interactions is great. Kava should not be used with other medications, particularly alprazolam, which may cause a semicomatose state (Almeida & Grimsley, 1996).

Kava is also contraindicated in patients with endogenous depression because it may increase the danger of suicide. It is also contraindicated during pregnancy and in lactating mothers. The herb should not be taken longer than 3 months unless under the supervision of a physician. It may potentiate the effectiveness of substances that act on the central nervous system such as alcohol, barbiturates, and psychopharmacological agents. There are also some concerns expressed in the medical literature that kava's use may, in some cases, be hepatotoxic (Escher, Desmeules, Giostra, & Mentha, 2001).

As opposed to functioning as a sole treatment agent, kava is proposed as an augment to psychotherapeutic treatment of panic. That is, the herb does not promote a cure but is best used as support in reducing anxiety while psychotherapeutic interventions are implemented. Also, because kava is not recommended to be used for more than 3 months, it may be limited to only short-term use.

Despite the limitations of this single-case example, this study suggests that kava may prove to be a potential alternative to pharmacotherapy in the treatment of panic. For this reason, large, double-blind, placebo-controlled studies are needed for future investigation in order to assess the true effects of the herb.

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