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# Need of Clinical and Mechanism-Based Preclinical Studies on the Efficacy of Nutraceuticals for Treating Brain Disorders

### Abstract

In recent years, the attention and direction of food science has been shifting from food safety and food flavor research to nutraceuticals and functional foods. Nutraceuticals is a broad term that describes products, which other than nutrition are also used as medicine. The present article discusses about the need of clinical and mechanism-based preclinical studies on the efficacy of nutraceuticals in treating brain disorders.

Keywords: Nutraceuticals; Brain; Pre-clinical; Clinical; Neurotransmitter; Memory; Depression

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### Introduction

The 'Nutritional Psychiatry' is a new field of research focused on the role of diet and nutrition in mental health [1]. Interest in the use of nutraceuticals and functional foods has risen substantially, largely because of their safety, adequate efficacy as well as potency [2].

Previously, it has been shown that various dietary patterns and different phytochemicals within traditional dietary foods have demonstrated many neuropharmacological properties in experimental models, which are predictive of human clinical efficacy [3]. It has been reported that oral administration of pomegranate extract (juice and seed extract) at dose of 10 mL/ kg body weight for 2 weeks significantly prolonged the summed immobility time during forced swimming test (an index of depression) in ovariectomized mice [4]. Oral administration of trans-resveratrol (40 and 80 mg/kg) produced antidepressantlike effect by regulating the central serotonin and noradrenaline levels and the related MAO-A activities in rats exposed to chronic stress [5,6]. Consumption of honey (100 g/kg) in diet for 52 weeks reduced anxiety and improved spatial memory in rats [7]. Other studies showed the use of honey as nutraceutical agents for treating anxiety, depression, convulsions, nociception, and hypnosis [8]. Consumption of soy-derived isoflavones via diet has antidepressant and anxiolytic effects in rats [9]. It has also been reported that consumption of a diet containing fish oil/omega-3 fatty acid docosahexaenoic acid (DHA), curcumin (an active component of turmeric), or a combination of both

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for 4 month improved cognitive deficits in 3xTg-AD mouse model of Alzheimer's disease [10]. Curcumin has been found to possess antidepressant action in various animal models of depression [11,12]. Blueberry supplementation (18.6 g dried aqueous extract/kg diet) has the potential to overcome genetic predispositions to Alzheimer's disease in transgenic mice from 4 months through 12 months of age [13].

Many nutraceuticals and functional foods like *Olea europaea*, *Nigella sativa*, and *Lycium barbarum* exhibit potential pharmacological effects against brain disorders in laboratory

studies, which are predictive of human clinical efficacy [2,14]. It has been reported that oral administration of Olea europaea (olive) oil (a major component of the Mediterranean diet) at doses of 0.25 or 0.5 mL/kg/day for 30 days, has neuroprotective effects in rats [15]. It also has anxiolytic, antidepressant, and memory enhancing effects in animal models [2,16]. Nigella sativa, commonly known as Black cumin or Black seed, has been traditionally utilized for culinary and therapeutic purposes [2]. Several studies showed that Nigella sativa (in a dose of 400 mg/kg body weight orally for 12 weeks) has neuroprotective effects as well as protects against memory impairments in rats [17,18]. It has also been shown that Nigella sativa has anxiolytic, antidepressant, as well as nootropic effects [2,19,20]. Thymoquinone, the main active component of Nigella sativa has also shown neuroprotective effects in rats [21]. Thymoquinone (20 and 40 mg/kg, i.p) have also shown improvement of stressinduced impairment of memory [22].

### Discussion

*Nigella sativa* and *Olea europaea* produce their beneficial effects through the modulation of neurotransmitters in the brain. These neurotransmitters in turn alleviate depression, anxiety, and help in memory enhancement [2]. Therefore, as mentioned above, nutraceuticals and functional foods have the potential to stimulate the central nervous system and protect the brain against various damages in preclinical studies [18]. However, the precise molecular and biochemical mechanism(s) underlying these pharmacological effects of nutraceuticals against various brain disorders has yet to be established.

On the other hand, various clinical studies have also demonstrated the efficacy of nutraceuticals in many mental disorders.

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Previously, it has been shown that *Nigella sativa* (one capsule of 500 mg once or twice daily for 4 or 9 weeks) has the potential for treating anxiety and stabilizing mood, enhancing attention and cognition in adolescent males [23,24]. Fish oil supplementation (7 capsules/day, each containing 320 mg fish oil) may also offer a safe strategy for attenuating post-traumatic stress disorder in women [25].

Most prescription drugs, such as antidepressants, antipsychotics, anxiolytics, and psychostimulants produce side effects [26]. This usually causes noncompliance in patients. An alternate for psychiatrists to overcome this noncompliance is to utilize safe alternative or complementary nutritional therapies [27].

### Conclusion

Evidence suggests that majority of nutraceuticals possess multiple pharmacological properties to help treat brain disorders. However, clinical and mechanism-based experimental studies on the use of these nutraceutical compounds in preventing and treating brain disorders are lacking. Moreover, many nutraceutical compounds clearly warrant formal preclinical drug development consideration for brain disorders to investigate the pharmacology of its components, to standardize the contents of the dosage forms, to define the methods of the pharmaceutical preparation, to determine its pharmacokinetics characteristics and its safety profile. Evidence-based research on nutraceuticals being marketed is needed to develop effective strategies for treatment of mental disorders.

## **Conflict of Interest**

There are no conflicts of interest.

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