

Herbal nootropics: *Crocus Sativus*, *Ginkgo Biloba* and *Melissa Officinalis*

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ABSTRACT

Nootropics are the substances which improve memory and cognition and ease learning. Consumers can benefit from nootropic plants as nutraceuticals, supplements and functional foods and beverages that improve mental functions. Nootropics can balance the neurological system and restore a sensation of relaxation and wellness leading to optimum self-healing and health. Although consumers are very new to the nootropic products interest in nootropic ingredients is increasing because people are looking for functional foods to enhance their attention, focus and memory and to manage their well-being and mood especially due to the Covid-19 pandemic. It is expected that these demands will continue, and nootropics market is estimated to increase to US \$5.32 billion with 13.2% compound annual growth rate (CAGR) by 2026 including pandemic impacts. Therefore, this mini review focuses on three of the natural herbal nootropics *Crocus sativus* (saffron), *Ginkgo biloba* and *Melissa officinalis* (lemon balm) as they are prominent ingredients in the functional product development.

KEYWORDS: Nootropics; *Crocus sativus*; Saffron; *Ginkgo biloba*; *Melissa officinalis*; Lemon balm; Mood; Cognition; Well-being

INTRODUCTION

Nootropics are the substances that ease learning and improve memory and cognition [1]. Nootropic is also mentioned as “acting on the mind” [2]. Consumers can benefit from nootropic plants and their extracted components in the form of nutraceuticals, supplements and functional foods and beverages that improve mental functions [3] offering mood boosting and cognitive benefits [4]. Nootropics can balance the neurological system and restore a sensation of relaxation and wellness resulting into optimum self-healing and health [2]. Even though nootropic products are still relatively new to the consumers, interest in nootropic products is growing as people seek functional foods to improve their attention, focus, and memory, as well as manage their well-being and mood, particularly including the effects of the Covid-19 pandemic. The market for nootropics was worth US \$1.96 in 2018, but with the impact of the pandemic, it is expected to grow to US \$ 5.32 by 2026, with a 13.2 % compound annual growth rate (CAGR) [4].

Natural and synthetic nootropic ingredients are both available. The most well-known and widely used nootropics in commercial

functional products include *Ginkgo biloba*, guarana, caffeine, *Melissa officinalis* (lemon balm), *Crocus sativus* (saffron) and turmeric, green tea, ginger, cocoa and B1, B6, B12 vitamins. Consumers are looking for cognition, memory and focus from their food and beverages [4]. According to the latest surveys, 56% of Gen Z customers in the United Kingdom are concerned regarding mental health consequences of using digital devices excessively and 73% of people in the United States who have had a mental health problem in 2020 have self-diagnosed [5]. Scientists are concentrating their efforts on studying herbal plants for medical purposes since they have less adverse effects and World Health Organization (WHO) has noted an increase in the usage of medicinal plants [6]. Consumers have a high sense of well-being and healthy living due to the pandemic now and it will continue in the future [5]. It is believed that functional foods and beverages formulated with nootropic ingredients (Table 1) help consumers for their mood, cognition and well-being. Therefore, three of the natural herbal nootropics, namely *Crocus sativus* (saffron), *Ginkgo biloba* and *Melissa officinalis* (lemon balm), are reviewed in this article since they are prominent ingredients in the functional product development.

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Table 1: Examples of functional food products formulated with herbal nootropics.

Product Information	Herbal Nootropic	Reference
Nootropic energy smart drink All-in-one energy shot with cognitive support	Product is mentioned to contain 3 mg of saffron stigma extract per serving (2 fl. Oz.)	Neurohacker [23]
Boost CBD drink, Mind+body boost	Product is stated to have 40 mg Ginkgo biloba	Aver [24]
Drug-free non-drowys holistic sleep drink solution, supports better sleep	Product contains lemon balm extract	Morelabs [25]

***Crocus Sativus* (Saffron)**

Crocus is a genus of flowering plants in the Iridaceae family that has about 85 species. *Crocus sativus* is one of the most studied of these species owing to the commercial manufacture of saffron from its stigmas and the related health advantages [6]. Saffron, which is coming from the Arabic word *azaferan*, is one of the most expensive herbs so it is also called as "red gold" [6,7]. *Crocus sativus* was traditionally used as a spice, colour and odour in Egypt and Rome. It has been used to reduce depression, relieve cramps, enhance sexual instinct, treat coughs, promote appetite, combat flatulence, induce sedation, suppress muscle spasms and ease respiratory congestions since old times [6]. *Crocus sativus* has been studied for its role as central nervous system (CNS) depressants, anti-asthmatic, emmenagogue and apoptogenic agents [8]. Crocin, saffranal and crocetin of *Crocus sativus* shows antioxidant and anti-inflammatory impacts on CNS [9]. *Crocus sativus* consumption is growing every day because of its pharmacological characteristics and potential therapeutic applications such as anti-depressant, cell formation and repair, digestive and blood cell production, antitumor, anticancer, antibacterial properties and treatment for Alzheimer's disease, cardiovascular disease and diabetes mellitus. So, this has led to cultivation of *Crocus sativus* globally [6,7]. In addition to its culinary usages, giving colour and aroma to food, due to the mentioned health benefits it has been started to include *Crocus sativus* in functional foods and beverages (Table 1).

Crocus sativus is a sterile triploid which generates yearly replacement corms and is propagated only from these corms. Corms are leafless during summer despite flower differentiation at this season. Pale lilac colour flowers are seen in fall or may occur before. The 3-part, brilliant red stigma, 25 to 30 mm length, droops over the perianth segments is the plant's most striking properties. Crocin gives the colour of saffron and its bitter taste and aroma is due to its saffranal and picrocrocin [10]. *Crocus sativus* consists of water, sugars, nitrogenous substances, soluble extracts, fibers and volatile oil [7]. Amount of each component depends on the origin of cultivation, growing conditions and fertility of soil [6]. Riboflavin and thiamine vitamins are abundant in this nootropic herb [7]. Stigmas of the plant contain different minerals such as calcium, iron, magnesium, potassium, sodium and phosphorous; whole flower of the plant and saffron spice bio residues have less fat and high amount of minerals and carbohydrates; and stamens have low amount of carbohydrates and high content of proteins and lipids. Major fatty acids in saffron are palmitic, linoleic and linolenic, as well as arachidonic, oleic and stearic acids [6].

Ginkgo Biloba

Ginkgo biloba (or ginkgo tree or maidenhair tree) is thought to be one of the most ancient species of trees. It belongs to Ginkgoaceae family [11]. *Ginkgo biloba's* Chinese name is "Yin-xing", which means "silver fruit". Its extracts from the leaves are used commercially. Memory loss and cognitive disorders, cancer, diabetes, ischemic heart disease and thromboses have all been

treated with the leaves of this plant [12]. *Ginkgo biloba* is used to boost mental energy via expanding blood flow to the cerebrum. It is known to offer nootropic effects as well as brain and cardiovascular benefits [13]. Some of the clinical applications of *Ginkgo biloba* are as follows: cerebral vascular insufficiency and impaired mental performance, Alzheimer's disease, depression, cognitive disorder, allergies, asthma, cochlear deafness, Raynaud's disease, tinnitus and high-altitude sickness [14].

The ginkgo tree is a deciduous tree with green leaves and these leaves turn into golden colour in fall season. The edible ivory-coloured seeds of ginkgo are inside the inedible foul odoured fruits produced by female trees [12,14]. *Ginkgo biloba* tree has a diameter of 3-4 ft with 100-122 ft height and lives up to 1000 years old. It has fan shaped leaves with 2-4 inches across. Ginkgo-flavone glycosides unique to the ginkgo, various terpene molecules peculiar to the ginkgo and organic acids are the active components of the leaves [14]. Chemical analysis of commercial *Ginkgo biloba* extracts obtained from the leaves varies from one producer to another due to a variety of factors such as processing, climate and strain [12]. There are a lot of types of *Ginkgo biloba* extracts commercially recently and mainly EGb761 and LI 1370 are the most used types in pre-clinical and clinical studies, especially EGb761 [11]. EGb761 type is available in Europe commercially, it contains two major groups of flavanol glycosides (24%) and terpene lactones (6%) [11,12] and has less than 5 ppm of ginkgolic acids and other components like proanthocyanadins, rhamnose, organic acids, glucose and D-glucaric [12]. Terpene ginkgolide B is thought to provide the mechanism of action of ginkgo as a neuroprotective agent, an antioxidant and a free radical scavenger [15]. EGb761 type is produced with extraction processes with 27 steps and the liquid extract obtained is dehydrated to 1 part extract from about 50 parts of raw leaves. Main flavonoids have been found as quercetin, isorhamnetin and kaempferol in the extract [12].

Ginkgo biloba extracts sales were more than US \$1 billion in 2020 for North America in 2020 [16] and they are available in various forms commonly available in herbal supplement shops and online. *Ginkgo biloba* can be bought as dietary supplements in many countries [12] and newly it has also been used in the formulations of functional products (Table 1).

***Melissa Officinalis* (Lemon Balm)**

Melissa officinalis (lemon balm) is a mint with square stems that are opposite to each other [17]. *Melissa officinalis* belongs to Lamiaceae family and is used in culinary, medicine and aromatic industries [18]. It is also used to add flavour to foods and beverages [19]. The leaves of the plant have a lemony odour when crushed/brushed. Balm word comes from "balsam" describing the herb's pleasant odour and genus name *Melissa* is derived from a Greek term for bees as they are very much attracted to lemon balm [17].

Melissa officinalis has long been used to treat particularly nervous system disorders and stress-related symptoms such as

moderate anxiety and insomnia and it is also used to relieve the symptoms of mild gastrointestinal problems like flatulence and bloating [20]. It has also been used for nervousness and dyspepsia in Europe for a long time and herbalist Culpeper mentioned *Melissa officinalis* as “opening the brain” in the 17th century [17]. Plant’s aerial portions are also used to cure headaches and rheumatism [19] and used as a sedative for depression, hysteria, insomnia and for heart palpitations due to nerves [17]. Lemon balm extracts and essential oils have been demonstrated to possess biological and pharmacological benefits including anti-bacterial, antioxidant, anti-viral, anti-fungal, neuro-protective, anti-diabetic, anti-tumor, insecticidal properties [19]. Use for Alzheimer’s disease [19], memory, agitation, irritable bowel syndrome, radiation protection and hyperlipidemia are some of the other clinical applications of *Melissa officinalis* [17]. Due to these benefits, especially in terms of nootropic properties, this valueable plant is used in supplements, plant-based pills and more recently in some functional food and beverage products (Table 1).

Melissa officinalis is native to southern Eurasia and western Asia. This perennial plant grows up to 1 m height and has 20-80 mm long hairy leaves. Lemon balm flowers are pale pink or white. *Melissa officinalis* may adapt to a variety of environmental conditions due to its hairy root system with several lateral roots [21]. Lemon balm grows at 15-35 °C quickly and needs 500-600 mm of well-distributed precipitation during the growth period [22]. Leaves of *Melissa officinalis* contains volatile oil and it is responsible for the lemon fragrance of the plant. This oil contains two types of terpenoids: hydrocarbon terpenes (such as citrals a and b) and sesquiterpenes (such as β -caryophyllene). Flavonoid glycosides are also very abundant in *Melissa officinalis* and rosmarinic acid makes up more than 3% of the lemon balm (dry weight) [17]. Yield of lemon balm, essential oil content and composition are impacted by many environmental and agricultural parameters and the differences could be attributable to growing conditions, genetic diversity and ontogenic period [21].

CONCLUSION

Nootropics have been used as medicine and treatment purposes due to their health benefits for many years, however commercial functional foods and beverages formulated with these valuable plants are few on the market. Although nootropic products are still relatively new to consumers, interest in nootropic substances is growing as people seek functional foods to improve their attention, focus, and memory, as well as manage their well-being and mood, particularly with the impacts of Covid-19 pandemic where anxiety, stress and sleep disorders have been seen. Therefore, herbal nootropics such as *Crocus sativus*, *Ginkgo biloba* and *Melissa officinalis* are potential ingredients to help people improve their mood, cognition and mental well-being when used in the product formulations. Scientific studies on the development of nootropic products are very limited in the literature. Hence, further research is required to enable functional nootropic product development and to contribute to the lives of the consumers.

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