ROLE OF HERBAL MEDICINES IN THE MANAGEMENT OF OBSESSIVE-COMPULSIVE DISORDER

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Abstract:
Obsessive-compulsive disorder (OCD) is a reasonably common mental illness that has a serious impact on the community's health. Although many patients find current conventional drugs to be effective, they can also have a variety of side effects. A variety of anxiolytic qualities have been found in substances derived from plants that have been tested for various mental diseases. We conducted a systematic evaluation of the pharmacological and clinical evidence of herbal medications and phytochemicals with antiobsessive-compulsive effects using the electronic databases PubMed, Scopus, and the Cochrane Library up to June 12, 2019, to assess the state of the evidence in the field. For the purpose of locating studies on the underlying mechanisms of action, additional search criteria were used. Results showed that numerous plant remedies, including *Crocus sativus*, *Citrus aurantium* L., *Silybum marianum*, *Withania somnifera* and *Echium*, have some tentative low-quality evidence.

Keyword: Herbal drug, obsessive compulsive disorder, phytochemicals.

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INTRODUCTION:

Like a brain damage, OCD frequently leaves its victims with lifelong problems. Obsessions (intrusive visions or thoughts) and compulsions (repetitive, ritualistic activities) are the two main manifestations of OCD. The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). OCD is not a symptom of a disease or caused by the effects of a drug, according to the diagnostic criteria in the DSM-IV. The diagnosis is changed to an anxiety disorder due to a general medical condition with obsessive compulsive symptoms when a specific biological factor directly responsible for an individual's presentation of OCD is identified (1). The lifetime prevalence of OCD is between 21% and almost 3% (2,3). Recent reviews of the epidemiology, pathophysiology, and therapy of OCD's neurobiology are available (2,4-9). OCD is sometimes thought of as a condition with many subgroups (7). Other scholars draw attention to the possibility that OCD is one of a range of diseases (8).

Although there is conflicting information regarding the neuroanatomical causes of OCD, it appears that cortico-striatal-thalamic-cortical circuits are crucial in mediating the condition (8). There is significant debate about the precise components that make up the basal ganglia, but these circuits are found in the frontal cortex, the basal ganglia, and the connections between the two. OCD has been linked to numerous neurological diseases involving these circuits, in addition to data from neuroimaging research (10-11). OCD that manifests for the first time beyond age 50 seems to be uncommon and is more likely to be linked to a neurological disorder(12). OCD is the fourth most prevalent mental illness, with diagnosis rates similar to those for diabetes mellitus and asthma (13). The coexistence of obsessions—uncon-trollable painful repeated thoughts, urges, or images—and compulsions—repetitive behavioural or mental acts carried out with the intention of reducing distress—characterizes this debilitating and disturbing mental health disorder (14). Genetic components and abnormalities of the central nervous system, particularly those affecting the serotonin, glutamatergic, and dopaminergic pathways, are involved in the pathophysiology of OCD. (15). In the general community, OCD has a lifetime prevalence rate of about 2% (16). having about equal numbers of men and women (15). According to certain research, affluent nations like the United States (1.3%) and Taiwan (0.4%) have a higher annual prevalence of OCD than developing nations like Taiwan (17). OCD impairs a patient's quality of life, which affects both their personal and professional lives (18). There are surprisingly limited therapeutic options given the large incidence of illness and its detrimental implications on socioeconomic status. Despite being a well-known treatment for OCD, cognitive behavioural therapy with the exposure and response prevention (ERP) approach is not always successful for all individuals (19). The first-line treatment for OCD is selective serotonin reuptake inhibitors (SSRIs), although about 40% of patients are resistant and do not respond (20).

Additionally, using SSRIs is linked to a number of negative side effects, including anxiety, sleeplessness, reduced libido, and sexual dysfunction (21). Potential sources of innovative pharmacological treatments for mental diseases include medicinal plants (22). For the treatment of OCD, Camfield et al. examined medicinal plants and phytochemicals (23). Researchers discovered a variety of botanicals that can treat this illness by altering two crucial pathways, including the glutamatergic and serotonergic pathways. However, because this study was done eight years ago, it is appropriate to give an update on the most recent data. Thus, the goal of this paper is to explore various herbal and phytochemical anti-OCD agents as well as their modes of action. A literature search was done to find any in vivo or clinical trials on the use of phytochemicals or herbal remedies to treat OCD.

METHODS

The preclinical and clinical information about plant medicines and OCD has been accessed up until June 12, 2019, according to the electronic databases PubMed, Scopus, and The Cochrane Library. English-language articles were included once language restriction was applied. The title, abstract, and keywords all contained the search phrases "obsessive compulsive disorder" or "obsessive" or "obsessive compulsive," as well as "herbal medicine" or "herbal" or "traditional" or "plant" or "phytomedicine" or "complementary." From the found articles, related articles were selected.

Duplicate articles, reviews, studies of obsessions other than OCD, and evaluations of complementary therapies other than plant-based therapies were also deleted. No limitations were placed on the study's scope, length, plant dosage, sample size, gender, or setting. The final included studies' references were checked for pertinent research. The final articles were examined to determine the scientific names of the plants, their parts and extracts, how OCD was presented, the type of clinical trial and animal model used, the number of participants, the interventions used, the length of the treatment, and

the effectiveness and tolerability of the herbal treatment for human studies.

RESULTS

Overview

18 papers from the 1022 that were located were used in this study. The final product included 7 human research and 11 animal studies. Trial durations ranged from 6 to 12 weeks, and the average sample size was 37 individuals (primarily studying cohorts). Each and every clinical study used using the Y-BOCS (Yale-Brown Obsessive-Compulsive Scale) to evaluate the OCD level. The Y-BOCS is a valid tool for assessing the intensity and recurrence of OCD patients' symptoms. A 10-item scale is used. that offers the time-related information that is important spent, obstruction, opposition, anxiety, and total control compulsions and obsessions (24). Each item is given a value between 0 and 4, and the total scores for all the items range from 0 (no symptoms) to 40 (very severe symptoms) (25). Herbal extracts were employed in all of the clinical trials that were included, albeit various extraction techniques were used. Although gender balance was almost universal in the trials, in several of them one gender was disproportionately overrepresented (26). Five of the seven clinical studies had been carried out in Iran and two in the US. Nine of the 11 preclinical research that examined obsessive-compulsive behaviours employed the marble-burying paradigm. This established animal paradigm does not require any pharmacological or behavioural modification to evaluate compulsive-like behaviour (27). In the marble-burying test, animals are put in a normal cage with 20 marbles arranged on top of a 5-cm depth of wood chip bedding. The amount of marbles buried is scored after 30 minutes (28). mCPP, nonselective serotonin receptor agonist, was used in one in vivo study to provoke OCD-like behaviour and assess Rats' overzealous self-grooming (29). The last research made advantage of quinpirole-induced compulsive checking and Animals were examined to determine behavioural indicators such as the number of visits to other animals, the frequency of stops, and the duration of total stopping. Items, as well as ritualistic behaviour frequency (30).

Herbal medicines and phytochemicals for OCD

Crocus sativus L. and *crocin*

Western Asia has traditionally valued the Iridaceae plant *Crocus sativus* (saffron) as a spice and medicinal. The stigma's neuromodulatory qualities, particularly as an antidepressant, are widely established in conventional Persian medicine (31). Saffron's psychotropic effects have been researched using a variety of animal and human clinical study models. It was acknowledged to have neuroprotective, calming, and antidepressant properties (32). Saffron has recently been speculated to offer anti-OCD properties. Fluvoxamine was compared to saffron extract (alone) in an RCT comprising patients with mild to moderate OCD. Saffron lowered Y-BOCS total score and obsessive subscale scores similar to those of fluvoxamine, according to the results. . After 10 weeks, the partial and total response rates for the saffron group were 69.56 and 34.7%, while for the fluvoxamine group they were 65.2 and 30.4%. These numbers did not differ substantially between the two groups ($p = 1$, $p = 1$). Although there was no discernible difference in the frequency of negative side effects between the two groups, the saffron-treated group had less headache, constipation, sweating, and vomiting. Although the precise mechanism by which saffron combats OCD is still unknown, it may include inhibiting serotonin reuptake in synapses (33). Saffron's neuro-protective properties against glutamate-induced damage were revealed by Bharate et al (34).

Additionally, its primary component, *crocin*, reduced L-glutamate-induced mitochondrial dysfunction and cell death in hippocampus neuronal cells (HT22) (35). Ettehadi et al., on the other hand, reported opposing effects of intraperitoneal injection of various doses of saffron aqueous extract on glutamate brain content in rats: a decreasing effect at 150 mg/kg and an augmenting effect at 250 mg/kg. It is important to note that the release of dopamine was increased in this study at doses of 50 to 250 mg/kg. However, norepinephrine and serotonin levels were unaffected by the extract (36). A new study suggests that crocin, an active ingredient in C. *sativus*, may be used to treat a variety of psychiatric problems. By healthy volunteers, it had been found to be safe when administered orally (37). In the light/dark rat model, crocin (50 mg/kg) demonstrated anxiolytic-like effects (38). It has been mentioned as a possible therapy for OCD management. There is only one in vivo investigation testing the anti-OCD characteristics of crocin in a rat model of OCD, and no clinical trial to support its efficacy. 1-(3-chlorophenyl) piperazine hydrochloride (mCPP), a nonselective serotonin (5-HT) receptor agonist, was used to cause excessive self-grooming. The findings showed that intraperitoneal crocin treatment could shorten the frequency and length of grooming. *Crocin* may operate as a 5-HT2C receptor antagonist, yet the precise pharmacological mechanism for how it affects obsessive behaviour is still understood. (39). Saffron and *crocin*'s high

antioxidant activity can be partly responsible for their neuropsychiatric effects. (40).

***Citrus aurantium* L.**

Rutaceae's *citrus aurantium*, sometimes referred to as bitter orange or orange flower, grows in tropical regions of Asia and has long been used to treat a number of medical conditions. Alkaloids, including synephrine, and flavonoids, particularly hesperidin and naringin, are the bitter orange's principal active phytochemicals (41). Anxiety has been reported to be successfully treated therapeutically using bitter orange volatile oil (42). The fruit essential oil has recently been touted as having anti-OCD properties. Limonene (97.83%) is the main chemical in bitter orange essential oil, while -myrcene (1.43%) is its secondary chemical. The central nervous system is naturally responsive to both of these substances. The 5-HT1A-receptor is thought to be responsible for these actions (43). According to Saketi, Bananej, and Jahromy (2014), bitter orange can strengthen serotonergic pathways and increase the impact of serotonin in synaptic clefts. lowers stress and obsessive-compulsive behaviour. Despite the lack of human trials, a mouse marble-burying test model was used for an in vivo investigation on bitter orange essential oil. The majority (97.83%) of the essential oil's constituents were limonene. According to the study, oral treatment of the fruit essential oil might stop mice from burying marbles (both in a single dosage for 30 minutes and in recurrent doses for 15 days) (44).

Withania somnifera* (L.) *Dunal

W. somnifera, a member of the Solanaceae family and often known as Indian Ginseng or Ashwagandha, has been a staple in Ayurvedic medicine for thousands of years. Researchers have looked at the adaptogenic, anxiolytic, antide-pressant, neuroprotective, and cognitive-improving properties of *W. somnifera* root. Due to its part in the downregulation of nNOS and the neurochemical modification of several neurotransmitter systems, it has been repeatedly demonstrated to increase neuroprotection (45). Numerous active components, such as withanolides, sitoindosides, and other alkaloids, are present in it. The presence of bioactive glycol-withanolids is thought to be responsible for the anxiolytic effects (46). Anxiety, serum cortisol, social dysfunction, and depression in individuals with a history of chronic stress were successfully decreased by 300 mg of *W. somnifera* root extract over the course of two months in an RCT including 64 patients (47). When *W. somnifera* root extract was given to OCD patients who were also taking SSRIs, the YBOCS score in the treatment group decreased significantly compared to the placebo group. The impact of *W. somnifera* on individuals with co-occurring anxiety disorders was also assessed in this study. The reduction in Y-BOSC score between patients with and without concomitant anxiety in each group was compared. These patients were examined individually in the treatment and control groups. Patients with or without concomitant anxiety saw similar reductions in Y-BOCS score in the treatment and control groups, respectively. No adverse events were reported during the trial, according to reports about the extract's safety (48). Although the effects of *W. somnifera* on OCD in this research are positive, a larger size RCT is necessary due to the small number of participants (15 patients in each group).

CONCLUSION:-

Administration of mCPP to rats caused increased self-grooming, which is consistent with earlier findings. Since treatment with these carotenoids had no influence on grooming activity at any of the tested dosages, a per se effect of *crocins* on grooming behaviour was not seen. *Crocins*, interestingly, decreased the excessive self-grooming caused by mCPP. But compared to their control counterparts, the mCPP and crocin-treated rats groomed more often. As a separate control for any direct pharmacological effects on physical activity that can cloud the interpretation of data from self-grooming, locomotor activity was measured. Similar levels of motility were seen in animals given mCPP and/or crocins, although these levels were lower than those seen in rats given vehicle + vehicle treatment. According to this pattern of findings, the effects of substances on rats' performance were unrelated to the level of motor activity. The new findings appear to be at odds with those of a prior study, which found that crocins had a sedative impact on mice because they decreased their grooming and motility. These contradictory results about the effects of crocins may be due to variations in the experimental conditions (type of animal, pharmacological design, behavioural procedure). More specifically, in that study, mice were utilised to investigate the effects of crocins, and a greater dosing regimen (50-600 mg/kg) than that employed in our experimentation was given 30 min before testing. We have not yet identified the pharmacological mechanism(s) that could explain how crocins affect obsessive behaviour.

To determine if the current findings apply to other species and behavioural paradigms, more research will be needed. The current research also supports a functional interaction between crocins and 5-HT

and shows how these active saffron components may contribute to compulsive behavior.

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