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EXPLORING THE THERAPEUTIC POTENTIAL OF SAFFRON EXTRACT IN THE MANAGEMENT OF STRESS

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ABSTRACT

Saffron, derived from Crocus sativus, is gaining research attention for potential therapeutic applications. Anxiety, stress, and low mood are closely related and may contribute to depressive symptoms. Among non-pharmacological solutions to improve subclinical mood symptoms and resilience to stress, natural products such as saffron—identified as promising following preliminary beneficial effects in major depressive disorder—represent a relevant strategy. saffron extract appears to improve subclinical depressive symptoms in healthy individuals and may contribute to increased resilience against the development of stress-related psychiatric disorders. Stress-related symptoms are a global concern, impacting millions of individuals, yet effective and safe treatments remain scarce. Although multiple studies have highlighted the stress- alleviating properties of saffron extract, the underlying mechanisms remain unclear.

KEYWORDS: Anxiety, stress, and low mood are closely related and may contribute to depressive symptoms.

INTRODUCTION

Saffron is the commercial name for the dried red stigmas of the *Crocus sativus* L. flower.[1] is appreciated for adding color, flavor, and a particular aroma to different food dishes or drinks (paella in Spain, Milanese risotto in Italy, lussekatter buns in Sweden, and alcoholic beverages). Saffron's principal producers are Iran and Spain, whereas the leading importers are Spain, Hong Kong, and the United States.[3] Saffron's quality is essential for consumers in the food industry.[7] and is based on the concentration of its apocarotenoids and their respective sensory attributes: crocin's coloring strength, picrocrocin's bitter taste, and

safranal's aromatic intensity. Saffron contains over 150 volatile and non-volatile compounds including proteins, carbohydrates, vitamins, amino acids, minerals, gums, and other compounds. However, the apocarotenoids (crocin, picrocrocin, and safranal) are responsible for saffron's sensorial attributes and are the major bioactive compounds used as markers for its quality. Furthermore, the quality and, consequently, the commercial value of saffron are based on the estimation of its coloring power, bitter taste, and aroma.[4]

Saffron's Chemical Composition

Saffron contains more than 150 compounds (volatile and non-volatile) including carotenoids (crocetin, crocin, β-carotene, lycopene, and zeaxanthin), monoterpene aldehydes (picrocrocin and safranal), monoterpenoids, and isopherones However, it also contains other compounds such as flavonoids, vitamins, proteins, and amino acids]. Saffron owes its sensory and functional properties mainly to the presence of its carotenoid derivatives, synthesized throughout flowering but also during the whole production process.[4] These compounds include crocin, crocetin, picrocrocin, and safranal, which are the secondary or bioactive metabolites Saffron's quality depends on its chemical profile and is directly related to the geographic area, climate variability, environmental practices, genetic traits, soil composition, cultivation conditions, and processing and storage methods. Nevertheless, according to the ISO standards (3632-1:2011 and ISO 3632-2:2010), the value and quality of the stigma are measured based on the content of the color components (crocin and crocetin), the bitter taste component (picrocrocin), and the volatile compounds responsible for the odor and aroma (safranal). These specific parameters are influenced by the environmental conditions, extraction method, purification, etc. Some studies have been conducted on the extraction of bioactive compounds from saffron using the concept of green chemistry. Some research on saffron stability demonstrates that temperature and humidity exert a strong influence on the degradation of the principal active ingredients.[8]

Stress can be defined as any type of change that causes physical, emotional, or mental strain. Stress is your body's response to anything that requires attention or action.

Everyone experiences stress to some degree. The way you respond to stress, however, makes a big difference to your overall mental and physical well-being.

When humans face a challenge or threat, they have a partly physical response. The body activates resources that help people either stay and confront the challenge or get to safety as fast as possible.

The body produces larger quantities of the chemicals cortisol, epinephrine, and norepinephrine. These trigger the following physical reactions.

- increased blood pressure
- heightened muscle preparedness
- sweating
- alertness

Stress is four types

1. Eustress: - Eustress is the "good" or "positive" stress that occurs in pleasurable settings. examples are the thrill of purchasing a new home, getting married, or the sensation you receive after a good workout.

2. Distress: - Distress is the negative or "bad" form of stress that arises when you consider stress to be hazardous, unusual, unjust, or painful. Job loss, the death of a loved one, long-term illness, catastrophic injury, divorce, and depression are all examples.

3. Acute stress: - Acute stress is a type of stress that lasts for a short period of time.

4. Chronic stress Eustress: - Chronic stress is a type of stress that lasts for a long time and persistent stress.

Three examples of types of stressors.

- routine stress, such as childcare, homework, or financial responsibilities
- sudden, disruptive changes, such as a family bereavement or finding out about a job loss
- traumatic stress, which can occur due to extreme trauma as a result of a severe accident, an assault, an environmental disaster, or war

SIGNS AND SYMPTOMS

1. Cognitive symptoms Memory problems, Inability or difficulty concentrating, Poor judgment Seeing only the negative, Anxious racing or ruminating thoughts.
2. Emotional symptoms Moodiness Irritability or shorttempered Agitation, inability to relax Feelings overwhelmed, Sense of loneliness or isolation,
3. Physical symptoms Aches and pains, muscle tension, Diarrhoea or constipation, Nausea, dizziness or butterflies in the stomach, Chest pain or rapid heartbeat, Loss of sex drive Frequent colds, Shallow breathing and sweating.
4. Behavioural symptoms Eating more or less, sleeping too much or too little, isolating yourself from others, Procrastinating or neglecting responsibilities, using alcohol, cigarettes, or drugs to relax, Nervous habits (nail biting, pacing).

Chronic stress has been reported to impair spatial learning and memory in a variety of spatial tasks. This effect is mediated mainly via the elevation of glucocorticoid levels (Conrad, 2010). It is well known that stress triggers the activation of the hypothalamus–pituitary–adrenal (HPA) axis, culminating in the production of glucocorticoids by the adrenal's glands. Receptors for these steroids are expressed throughout the brain, and expression is particularly strong in brain structures involved in cognition and mental health, including the hippocampus (De Kloet et al., 1987, Reul and deKloet, 1985). Glucocorticoids can have short and long-lasting effects on behavior and cognitive functions via genomic and non-genomic mechanisms (Haller et al., 2008, Lupien et al., 2009). In fact, chronic stress induces a series of morphological changes in the hippocampi of rats and primates. These alterations include retraction of the apical dendrites in the CA3 region of the hippocampus, modification of hippocampal dendritic spine number and shape, and cell death (Conrad et al., 2007, Kleen et al., 2006).

When the hypothalamus encounters a threat it performs some specific functions: 1. activates autonomic nervous system (ANS) 2. Stimulates Hypothalamic Pituitary Adrenal (HPA) axis by releasing Corticotrophin Releasing Hormone (CRH) and 3. Secrets arginine vasopressin

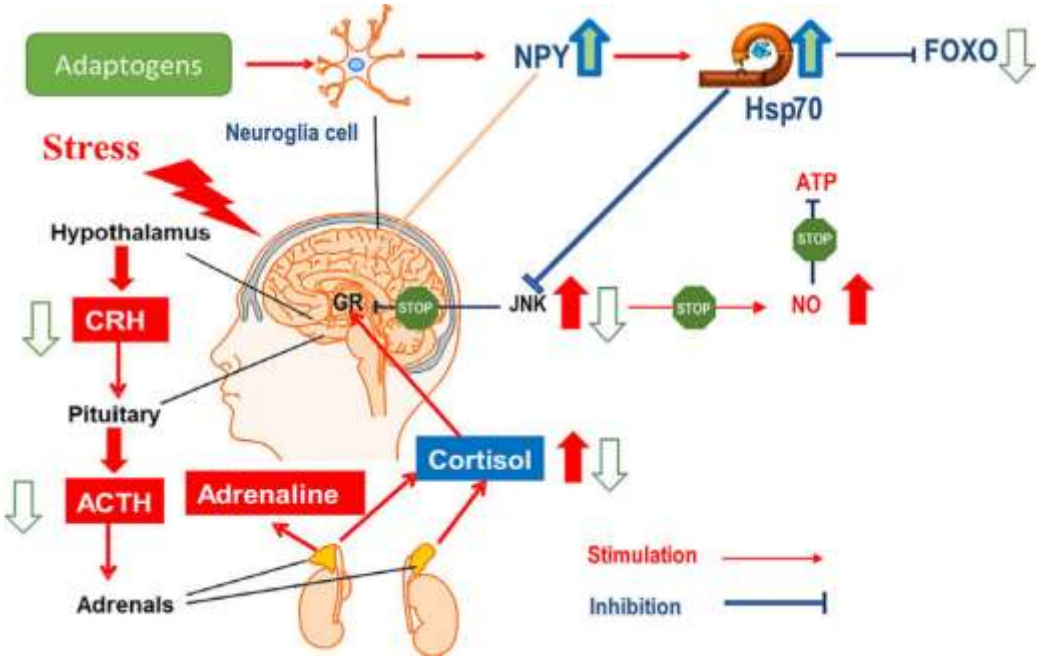
(Antidiuretic Hormone ADH). Autonomic nervous system consists of sympathetic (arousal) and parasympathetic (relaxed) nervous system. The ANS regulates visceral activities like circulation, digestion, respiration, temperature regulation and some vital organs How to treat anxiety naturally.

The sympathetic system accounts for the flight-or-flight response. In response to a stressor catecholamines: epinephrine (adrenaline) and norepinephrine (nor adrenaline) are released at various neural synapses. The release of these catecholamines causes several changes like increase in the heart rate and force of myocardial contraction vasodilatation of arteries throughout working muscles and vasoconstriction of arteries to nonworking muscles; dilation of pupil and bronchi and reduction of digestive activities in the body. All these changes are required to prepare the body for fight-or-flight response. The effects of these hormones - epinephrine and nor epinephrine last for few seconds. The functions of parasympathetic nervous system are opposite to that of sympathetic nervous system and help in energy conservation and relaxation.

CRH acts at the anterior pituitary gland an endocrine gland located in the brain. Pituitary gland is also called ‘master gland’, as it controls the secretion of other endocrine glands in the body. On stimulation by CRH, anterior pituitary secretes Adrenocorticotropin Hormone (ACTH). According to Scantamburlo et al., arginine vasopressin modulates the effect of CRH on ACTH secretion.[2]

ACTH released from anterior pituitary gland in response to CRH stimulates adrenal glands located on the kidneys.

ACTH stimulates adrenal cortex to release corticoids (glucocorticoids and mineralocorticoids). The major function of glucocorticoids is to release energy, which is required to cope with the ill effects of stressor. The energy is released by conversion of glycogen into glucose (glycogenolysis) and also by breakdown of fats into fatty acids and glycerol (lipolysis). In addition to this corticoids have several other functions such as: increased urea production, appetite suppression, suppression of immune system, exacerbation of gastric irritation, associated feeling of depression and loss of control.



These are the symptoms generally seen in a person under stress. Mineralocorticoid (aldosterone) promotes Na+ retention and elimination of K+. It increases blood pressure by increasing blood volume. The medulla part of the adrenal gland secretes epinephrine and norepinephrine. The functions of these hormones are the same as that of those secreted from nerve endings of sympathetic nervous system. These hormones secreted by adrenal medulla, reinforce the functions of sympathetic nervous system. The release of these hormones from adrenal medulla acts as a backup system to ensure the most efficient means of physical survival. The effects brought out by epinephrine and norepinephrine from the sympathetic nervous system may be termed as immediate effects and the effects brought out by those of adrenal medulla are intermediate effects.

Management of Stress Naturally

1. Exercise

Studies show that physical exercise can help reduce anxiety symptoms.

2. Meditation

Meditation can help to slow racing thoughts, making it easier to manage stress and anxiety. A wide range of meditation styles, including mindfulness and meditation during yoga, may help.

3. Relaxation exercises

Some people unconsciously tense their muscles in response to anxiety. Progressive relaxation exercises can helpTrusted Source to alleviate this tension and reduce stress.

4. Journaling

Finding a way to express anxiety can make it feel more manageable.

5. Time management strategies

Some people feel anxious if they have too many commitments at once. These may involve family, work, and health-related activities. Having a plan for the next necessary action can help keep this anxiety at bay.

6. Aromatherapy

Smelling soothing plant essential oils can help to ease stress and anxiety. Certain scents work better for some people than others, so consider experimenting with various options.

7. Herbal teas

Many herbal teas promise to help with anxiety and ease sleep. Some people find making and drinking tea soothing, but some teas may have a more direct effect on the brain that results in reduced anxiety.

REVIEW OBJECTIVES

1. **Evaluate Efficacy:** Determine the effectiveness of saffron extract in reducing stress levels. overall stress resilience in individuals consuming saffron extract.
2. **Understand Mechanisms:** Investigate the biological and psychological mechanisms by which saffron extract influences stress and its impact on neurotransmitter levels, hormonal responses, and brain activity associated with stress management.
3. **Assess Safety:** Evaluate the safety profile of saffron extract. Monitoring for any adverse effects, interactions with other medications, and long-term safety in various populations.
4. **Determine Optimal Dosage:** Identify the most effective dosage and form of saffron extract for stress relief. This involves testing various doses and formulations to find the optimal balance between efficacy and safety.
5. **Explore Synergies:** Investigate the potential for saffron extract to be used in combination with other stress-reducing therapies, whether they are pharmacological, psychological, or lifestyle-based, to enhance overall therapeutic outcomes.

LITERATURE REVIEW

- **Pouchieu Camille et al**. This study reports that a single dose of Safr'InsideTM in healthy young men delayed the typical peak of salivary cortisol and cortisone appearing in response to a physical and psychosocial stressor, in comparison to a placebo. This interesting finding therefore supports the biological role of Safr'InsideTM in the stress management. In addition, we also showed, for the first time in a human study, that Safr'InsideTM and its main volatile compound safranal may reduce the level of perceived stress and anxiety, although the underlying biological mechanism needs further investigations.
- **Philippa A. Jackson et al.** The current study explored the effects of a proprietary saffron extract (Safr'InsideTM) on emotional well-being following 14,28, and 56 days supplementation in healthy adults experiencing low mood as measured using the POMS. Effects of the extract on physiological and psychological response to a psychosocial stressor (OMS) were also measured following a single acute dose and postdose at the time points mentioned above. The results revealed several beneficial effects of saffron on subjective mood and quality of life measures, with the clearest finding reflecting a greater reduction in the depression scale of the POMS compared to placebo. This was accompanied by an improvement in social relationships on day 56.

- **Nanda Sanju et. Al.** Safranal, a natural antioxidant chemical from saffron (Crocus sativus) has been reviewed in this paper. Safranal, crocin and other apocarotenoids also offer therapeutic use in oxidative stress diseases as given by various clinical and non-clinical studies.

Golpour- Hamedani et al. Saffron compounds might improve antioxidant defense and oxidative stress, and reduce Aβ deposits as the most important mechanism of the progression of neurodegenerative diseases. However, limited information is available to make any suggestion regarding the effect of saffron on all disorders. Trials with an adaptive design and providing exclusive results are needed to confirm the effects of saffron and its compounds to help decide on the effectiveness of saffron supplements in neurodegenerative diseases.

- **Xin Su et al**. saffron extract can inhibitthe occurrence of oxidative stress by protecting vascularendothelial and myocardial cells and normalizing the hyper-sensitive oxidative stress. As a traditional medicine, saffron has been widely used since many ages in clinical prac-tice. Therefore, it is necessary to study the effective compo-nents of saffron, such as crocin, crocetin, and safranal.
- **Wolfgang Marx et al.** Twenty-three studies were included. Saffron had a large positive effect size when compared with placebo for depressive symptoms ($g = 0.99$, $P < 0.001$) and anxiety symptoms ($g = 0.95$, $P < 0.006$). Saffron also had a large positive effect size when used as an adjunct to antidepressants for depressive symptoms ($g = 1.23$, $P = 0.028$). Egger's regression test found evidence of publication bias.
- **Xin Su et el.** Review Article The Beneficial Effects of Saffron Extract on Potential Oxidative Stress in Cardiovascular Diseases.
- **J. Brettschneider et el.** Spreading of pathology in neurodegenerative diseases: a focus on human studies, Nat. Rev. Neurosci. 16 (2) (2015) 109–120. [2] R. Pal, J.P. Larsen, S.G. Moller.
- **Adrian L Lopresti et al.** An examination into the mental and physical effects ofa saffron extract (affron®) in recreationally-active adults:A randomized, double-blind, placebo-controlled study, 2022; 19(1): 219–238.
- **Geetanjali1 al.** (April 2023) Exploring Effective Strategies for Stress Management: Enhancing Mental Well-being through Mindfulness, CBT, Exercise, and Relaxation Techniques, 12: 345-348.

- **Chae-Young Kim et. al.** (2023): Effects of Saffron Extract (Affron®) with 100 mg/kg and 200 mg/kg on Hypothalamic-Pituitary-Adrenal Axis and Stress Resilience in Chronic Mild Stress-Induced Depression in Wistar Rats.

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