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Mini Review

Novel Extraction of Bioactive Compounds from *Crocus sativus*: A Mini Review

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ABSTRACT

Crocus sativus L. is a valuable medicinal plant that is widely produced for both nutritional and commercial purposes. Saffron and its components have significant pharmacological properties and the potential to display a wide range of therapeutic effects. Saffron contains a high concentration of bioactives such as crocins, crocetin, safranal, picrocrocins, essential oils, and minerals. Obtaining any important substances, such as bioactive chemicals found naturally in plants, is entirely dependent on extraction and purification techniques. The green chemistry requirements for a successful bioactives extraction process should be met, including those for efficiency, economy, or at least minimal contaminants, and safety. The bioactives from saffron have been extracted using a variety of techniques, either separately or in combination, including conventional routes (such as solvent extraction and maceration) and contemporary procedures (e.g. supercritical fluids, pulsed electric field, emulsion liquid extraction, microwave, sonication, enzyme assisted extraction, etc.). The focus of the current review is on the cutting-edge extraction of saffron's bioactive components, which could produce products with an additional value from the most costly spice in the world for uses in food, medicine, and cosmetic formulations.

Keywords: *Crocus sativus*; Saffron; Modern extraction; Bioactivesl; Cosmetics

INTRODUCTION

Due to their low prevalence of negative effects, medicinal plants are regarded as one of numerous essential and useful techniques for health intervention. Saffron, also referred to as *Crocus sativus* L. (Iridaceae), is a crucially important medicinal and aromatic plant. The dry stigmas of the saffron plant are what give the spice the nickname "golden condiment" and make it the most expensive spice in the world [1]. Because each stigma weighs roughly 2 mg, 1 kg of saffron requires approximately 150,000 flowers. Saffron has a harsh flavor and a strong hay-like aroma. Picrocrocin, a glycosylated monoterpenoid chemical, is primarily responsible for the bitter taste, and safranal, a monoterpenoid substance, is primarily responsible for the hay-like odor. The most significant bioactive compounds in saffron extract, according to chemical analysis, are crocin, crocetin, safranal, and picrocrocin.

It has been established that the phytochemicals in saffron, such as crocin, picrocrocin, and safranal, are beneficial to health. The therapeutic uses of saffron have been the subject of numerous investigations. Saffron has been discovered to be important in the treatment of several illnesses, including asthma, depression, menstrual disorders, cardiovascular disease, digestive issues, cancer, insomnia, antispasmodic, aphrodisiac, diaphoretic, and several other conditions [2]. It has been demonstrated through experimentation that *C. sativus* is useful for treating Premenstrual Syndrome Symptoms (PMS). In ayurvedic medicine, it has been used as an expectorant, emmenagogue, and adaptogenic agent. Saffron was utilized by the ancient Greeks to treat wounds, acne, and other skin issues. Because of its moisturizing qualities and high antioxidant content, saffron is frequently used in fragrances, cosmetics, and the treatment of skin cancer [3].

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LITERATURE REVIEW

Extraction

To use bioactive substances in foods and nutraceuticals that promote good health, it is essential to extract them from various plant compartments. In comparison to conventional approaches, it is claimed that a suitable extraction pathway can gather the desired bioactives up to five times. The type of bioactive substances present in the researched plant and the inherent characteristics of the plant should be taken into consideration when choosing an extraction process from the classic to the advanced ones.

Extraction and purification techniques are absolutely necessary to obtain any important substances, such as bioactive chemicals that are naturally found in plants. An effective extraction process for bioactive chemicals should satisfy the following criteria: Efficiency, economy, run-down or at least minimal contaminants, safety, and environmental friendliness. A crucial stage in their subsequent isolation and fractionation is the extraction of bioactive chemicals [4]. It has been claimed that the saffron's bioactive components' quality and amount are significantly influenced by the extraction process. As a result, numerous alternative extraction techniques have been used singly or in combination to extract valuable bioactives from the saffron parts.

A range of extraction methods, from traditional to novel, have been used to extract bioactive compounds from various parts of the saffron plant. Traditional bioactive material extraction processes, on the other hand, have major limitations in terms of the volume of hazardous solvent used, the duration of the extraction time, and the high temperature of processing. Because of the limits of existing methods, new novel extraction technologies known as "green technologies" are being developed [5]. These innovative extraction technologies are non-toxic, effective, long-lasting, environmentally safe, quick, and target-specific. The progression of contemporary extraction technologies for bioactive components from the saffron plant in chronological order is addressed under.

Super Critical Fluid Extraction (SCFE)

These Super Critical Fluids (SCF) have a high diffusivity across solid materials, which allows for quick extractions. Because it is nontoxic, has a low critical temperature, and creates an environment free of oxygen, carbon dioxide is commonly utilized as a supercritical solvent. Because CO_2 is less polar, it is easier to include non-polar bioactive chemicals like the safranal in saffron [6]. Polar bioactive components like crocetin and crocin from saffron are extracted *via* the use of co-solvents such as ethanol, methanol, or water. Came to the conclusion that using SCFE and water as a co-solvent increased the yield of saffron's glycosylated bioactives like picrocrocin, 4-Hydroxy-2,6,6-Trimethyl-4-Hydroxy-1-Carboxproducts (HTCC), and crocin [7]. Safranal and deglycosylated crocin are produced in greater proportions when methanol is used as a co-solvent during extraction. Dehydrating HTCC also results in the production of safranal. Due to HTCC's conversion to safranal by dehydration, the yield of safranal increases at higher temperatures. Crocin and picrocrocin derivatives had the best yield at 80°C and 30 MPa, whereas safranal and HTTC produced the highest yield at 40°C and 40 MPa [8].

Ultrasonic-Assisted Extraction (UAE)

Mechanical waves with frequencies between 20 MHz and 100 MHz are used in the ultrasonic extraction process. Because acoustic cavitation involves the compression and stretching of liquid molecules, it is primarily responsible for the effects of ultrasonication during extraction in a liquid medium. Cavitation, which leads to the production of voids or bubbles, takes place when the intermolecular spacing between liquid molecules is greater than a predetermined threshold. As long as the ultrasonic intensity is kept at a specific low level, these oscillating bubbles usually remain stable. A temperature of a thousand degrees and a pressure of more than 1000 atmospheres will be produced by these cavitation bubbles. These cavitation bubbles burst near or onto the surface of the extraction material during extraction, creating high-velocity liquid jets. To release entrapped bioactive chemicals from plant sources, the ultrasonic extraction method has been frequently used [9]. The key operational parameters impacting extraction yield during ultrasonic extraction are frequency, temperature, ultrasonication time, and kind of raw material. High yield, low energy usage, a shorter extraction time, and the use of solvents are benefits of UAE over conventional extraction.

For the extraction of bioactive components from the saffron plant, several researchers have used ultrasonication either on their own or in conjunction with other techniques. Numerous bioactives, including crocin, picrocrocin, safranal, and flavonoids (quercetin, kaempferol), have been extracted from saffron in the UAE. Results from the study showed that UAE was more effective than maceration. According to the study, an optimal extraction can be accomplished in ten minutes, which helps shorten extraction times. UAE extraction produces less heat and doesn't significantly alter the nature of the bioactive ingredients. Ahmed researched the antioxidant and antibacterial properties of an ultrasonic-assisted saffron tepal extract made of glycosylated and aglycon flavonoids.

For hydrolyzed and non-hydrolyzed petal extract, the total phenolic content was found to range between 5.5 ± 0.9 mg and 31.3 ± 0.8 mg Caffeic Acid Equivalents/g (CAE/g). In addition, the extract demonstrated antibacterial action at concentrations as low as 1.5 mg [10].

Microwave-Assisted Extraction (MAE)

Since microwaves are electromagnetic, they allow for the opposite of what happens during the conventional extraction-the flow of heat and mass from the interior of the raw material to the solvent medium. Due to the material's rapid volumetric dispersion throughout the food during microwave heating, the temperature rises quickly. Ionic conduction, dipole rotation, and localized radiation heating all contribute to this heating [11]. As a result, pressure builds inside the cells, causing the cells' bioactive components to be extracted and dissolved in the solvent. Conducted a study on the optimization of MAE process parameters for the extraction of saffron bioactives (picrocrocin, safranal, and crocin). The ideal conditions for extracting the bioactives from saffron were 95.91°C, 30 min, and 59.59% ethanol concentration. Optimization study on MAE using RSM showed that it was a quick and effective method for removing anthocyanins from saffron petals [12]. Additionally, it was discovered that MAE considerably reduces the extraction time. Showed an increase in total phenolic content extraction with increasing power from 100 W to 500 W [13]. Several research has shown that reducing the extraction time, the amount of solvent required, and increasing the yield of bioactive components of MAE over other methods has advantages.

Pulsed Electric Field Extraction (PEFE)

In this method, high-intensity electric field pulses (20 kV/cm to 80 kV/cm) are typically used to extract bioactive components from plant material. PEF is regarded as a non-thermal and energy-saving approach that needs less time and energy to extract and process while just slightly altering the bioactive chemicals. A cell's permeability for the release of bioactive components is increased by electroporation, which occurs when an electric field develops across the cell membrane and abruptly breaks down. Comparing PEFE to traditional extraction, more methyl xanthines and polyphenols were produced.

There hasn't been much study on PEF extraction's ability to extract bioactive components from saffron. Compared to that produced by solvent extraction, revealed an increase in the release of crocin, safranal, and picrocrocin content of the stigma by 14%, 15.5%, and 10.2%, respectively. The study came to the further conclusion that extraction of apocaroteniods from saffron at room temperature (25°C) results in considerable pore development when pulses of 1 KV/cm-5 KV/cm are used.

Emulsion Liquid Membrane Extraction (ELME)

Emulsion Liquid Membrane (ELM) is a cutting-edge extraction method with higher selectivity and less solvent use. Because it doesn't require heating and uses the least amount of energy, the membrane approach is becoming more popular for the extraction of bioactive components. The phrase "bubble within a bubble" describes ELM. While extractants are present in the outside bubble, internal phase reagent is present in the inner bubble. As the concentration gradient activity of the target molecule in the internal phase is kept close to zero, the solutes from the aqueous phase go to the stripping phase. Depending on the characteristics of the donor phase and acceptor phase, the emulsion systems may be two-phase, such as Water-in-Oil (W/O) or Oil-in-Water (O/W) types, or three-phase systems, which comprise either W/O/W or O/W/O. The procedure depends on the membrane phase's proper composition, which includes selecting the right organic phase, internal phase, diluents, emulsifier, and extractant compositions.

To extract crocins, safranal, and picrocrocin from the saffron stigma using nano-emulsion membranes, carried out a study to optimize several parameters, including surfactant type, the concentration of surfactant, type of diluent in the membrane, mixing speed and phase, and treat ratios. According to the study's findings, the ideal conditions for extracting saffron apocarotenoids are span 80 at a 2.5% surfactant concentration, n-decane as a membrane diluent, treatments, and phase ratios of 0.3 and 0.8, respectively.

Enzyme-Assisted Extraction (EAE)

Enzymes acting on plant material's cell walls hydrolyze them, which encourages the release of hydrophilic and hydrophobic bioactive components from plant cells. This is the fundamental mechanism of enzyme-mediated extraction. The method is best suited for heat-sensitive components and also favors reduced time and energy consumption.

Lotfi et al., investigated the extraction of anthocyanins from saffron petals using cellulase, hemicellulase, and pectinase enzymes at various doses and times. In comparison to anthocyanins (pelargonidin 3, 5-glucosides) obtained by solvent extraction in ethanol, it was discovered that anthocyanins (cyanidin 3-glucosides) obtained *via* enzyme extraction have three times better heat resistance. The key factor contributing to the enzyme extract's increased stability is its higher concentration of cyanidin 3-glycosides.

Subcritical Water Extraction (SWE)

At temperatures between 100°C and 374°C, pressurized water is used to achieve the extraction. The extraction process benefits from the high pressure because it keeps the water in a liquid form. Under subcritical circumstances, the strength and structure of hydrogen bonds, among other thermodynamic properties of water, are impacted. Water's hydrogen bond strength is reduced by the high temperature under subcritical circumstances, which also reduces water's polarity and dielectric constant. Water's polarity under subcritical conditions is comparable to organic solvents (such as ethanol and methanol) under ambient temperature. Thus, nonpolar compounds become more soluble in water under subcritical circumstances. Due to the high temperature, which improves diffusivity and mass transfer under subcritical circumstances, water's viscosity and surface tension also drop. There are four steps in the SWE process. The target analyte is first dissociated from plant matter. The solute in the water dissolves as the subcritical water then permeates the plant material. The solute is finally removed from the plant matrix.

Ahmadian-Kouchaksaraie, et al., investigated phenolic component extraction by SWE from saffron flowers. For the extraction of phenolic chemicals, the study included parameter optimization for temperature, Water-to-Solid (W/S) ratio, and extraction duration. In terms of total flavonoid content (239 mg/100 g), total phenolic content (1616 mg/100 g), FRAP value (5.1 mM), and percent DPPH activity (86.05%), the extraction at 159°C for 54 min and Water to Solid (W/S) ratio of 36 mL/g produced the best results. Esmaeelian et al., researched the SWE extraction of bioactive components from saffron corm using RSM. To assess the antioxidant activity and total phenolic content of corms, the extraction duration, and temperature in the range of 100°C-180°C and 10 min-30 min were examined.

At 180°C and 21.99 minutes, the highest levels of antioxidant and total phenolic activity were discovered and conducted a second SWE investigation on the bioactives in saffron by adjusting the temperature and time of the extraction. We looked at the extraction yield of picrocrocin, safranal, and crocin at temperatures and times between 5 minutes and 15 minutes and 102°C and 125°C. The temperature and duration that produced the highest production of these bioactive substances were 105°C and 7.32 min, respectively.

High Hydrostatic Pressure Extraction (HHPE)

HHPE is a non-thermal process that uses high-pressure (100 MPa–1000 MPa) application to boost the production and quality of bioactive components. Since the approach primarily disrupts non-covalent bonds, hydrogen, electrostatic, hydrophobic bonds, and van der waals interactions, it has no detrimental effects on the structure of low molecular weight compounds. The extraction of bioactive components from saffron was studied utilizing the HHPE method at a pressure range of 100 MPa-600 MPa and a temperature range of 30°C-70°C. It was discovered that as the pressure increased, the extraction yield increased as well. The yields of the bioactives crocin, safranal, and picrocrocin increased by 52% to 63%, 55% to 62%, and 54% to 85%, respectively. With rising temperatures, a drop in crocin content from 25% to 36% was also noted. The ideal conditions were discovered to be 580 MPa, 50°C, and 5 minutes, respectively.

Ohmic Heating-Assisted Extraction (OHAE)

The process relies on heating food by causing it to oppose the flow of electrical current, which transforms electrical energy into thermal energy. When it comes to bioactive compounds like phenolic compounds and carotenoids, etc., this heating procedure can be regarded as less harmful than standard thermal processes. Because ohmic heating requires less time to process and produces more bioactive components, it seems to be a good extraction technique. It is regarded as a quick, reliable, energy-saving, and environmentally friendly technique of heating.

Conducted a relative investigation on the extraction of bioactives by OHAE, MAE, and UAE from saffron petals. The study suggested using OHAE as the best method for extracting bioactive compounds from saffron petals. Total phenol and flavonoid content rose with an increase in voltage up to 225 V and OHAE extraction period up to 45 min.

RESULTS AND DISCUSSION

Due to its beneficial qualities derived from its bioactive ingredients, saffron has been widely utilized in a variety of industries, including the culinary, cosmetics, and pharmaceutical sectors. The bioactive substances in saffron are quite sensitive to environmental conditions like pH, light, oxygen, enzyme, and heat, etc. To enhance extraction efficiency, it is strongly advised to choose appropriate extraction methods based on modern technologies like HHPE, PEFE, OHAE, and EAEE. The current mini-review aims to succinctly outline recent developments in the extraction of saffron's bioactive components, which could lead to value-added products from the world's most expensive spice for uses in food, medicine, and cosmetic formulations. The majority of research investigations conducted to date have been on the isolation, characterization, and use of bioactive components from saffron stigma. However, more study is needed to determine how cutting-edge extraction techniques affect the bioactives from the floral biomass of the saffron plant, as their potential has not been investigated.

CONCLUSION

This study explored the effects of different processing parameters such as time, temperature and ethanol concentration in MAE on saffron floral by-products, in terms TPC, TFC and antioxidant activity (ORAC and HOSC assays). At laboratory scale, the results showed that the optimal MAE conditions for the extraction bioactive compounds were using ethanol as primary solvent (50% or 100%) and low temperatures. Therefore, this information could help to choose the most appropriate extraction method and parameters to obtain compounds of interest from natural plant sources, including scale-up to industrial level.

From these findings, it can be concluded that MAE was an efficient technique that allows obtaining high added value compounds from saffron floral by-products with low energy footprint. Additionally, this research provides new information about the functional compounds present in saffron floral by-products extracts, representing an important source of natural antioxidant compounds and that could be considered as a source of promising bioactive ingredients for the development of functional foods and for other human health applications.

CONFLICT OF INTEREST

The authors declare they have no conflict of interest.

REFRERENCES

1. Shahi T, Assadpour E, Jafari SM. Main chemical compounds and pharmacological activities of stigmas and tepals of ‘red gold'; saffron. Trends Food Sci Technol. 2016;58:69-78.
2. Mzabri I, Addi M, Berrichi A. Traditional and modern uses of Saffron (*Crocus sativus*). Cosmetics. 2019;6(4):63.
3. Garavand F, Rahaee S, Vahedikia N, Jafari SM. Different techniques for extraction and micro/nanoencapsulation of saffron bioactive ingredients. Trends Food Sci Technol. 2019;89:26-44.
4. Khaw KY, Parat MO, Shaw PN, Falconer JR. Solvent supercritical fluid technologies to extract bioactive compounds from natural sources: A Review. Molecules. 2017;22(7):1186.
5. Bakshi RA, Sodhi NS, Wani IA, Khan ZS, Dhillon B, Gani A. Bioactive constituents of saffron plant: Extraction, encapsulation and their food and pharmaceutical applications. Appl Food Res. 2022;2(1): 100076.
6. Gahruie H, Parastouei K, Mokhtarian M, Rostami H, Niakousari M, Mohsenpour Z. Application of innovative processing methods for the extraction of bioactive compounds from saffron (*Crocus*

sativus) petals. J Appl Res Med Aromat Plants. 2020;19:100264.

7. Khan HW, Reddy AVB, Nasef MME, Bustam MA, Goto M, Moniruzzaman M. Screening of ionic liquids for the extraction of biologically active compounds using emulsion liquid membrane: COSMO-RS prediction and experiments. J Mol Liq. 2020;309:113122.
8. Fan L, Fan W, Mei Y, Liu L, Li L, Wang Z, Yang L. Mechano-chemical assisted extraction as a green approach in the preparation of bioactive components extraction from natural products-A review. Trends Food Sci Technol. 2022;129:98-110.
9. Lotfi L, Kalbasi-Ashtari A, Hamedi M, Ghorbani F. Effects of enzymatic extraction on anthocyanins yield of saffron tepals (*Crocus sativus*) along with its color properties and structural stability. J Food Drug Anal. 2015;23(2):210-218.
10. Cheng Y, Xue F, Yu S, Du S, Yang Y. Subcritical water extraction of natural products. Molecules. 2021;26(13):4004.
11. Esmaeelian M, Feizy J, Jahani M, Einafshar S. Evaluation of different extraction methods on the antioxidant and antibacterial properties of the saffron corm extract. Saff Agr Tech. 2021;9(3):269–284.
12. Sarfarazi M, Jafari SM, Rajabzadeh G, Galanakis CM. Evaluation of microwave-assisted extraction technology for separation of bioactive components of saffron (*Crocus sativus* L.). Ind Crops Prod. 2020;145:111978.
13. Huang HW, Hsu CP, Yang BB, Wang CY. Advances in the extraction of natural ingredients by high-pressure extraction technology. Trends Food Sci Technol. 2013;33(1):54–62.