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A review on Saffron as magic flower proved by modern techniques

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ABSTRACT: Saffron is considered as a golden crop all over the world due to its reddish aromatic stigma. Saffron is also considered as a king of Spices. Due its high price it is always subjected to adultration.it is widely grown in Jammu and Kashmir in India. The main chemical constituents present in saffron are crocin, picrocrocin, and Safranal. Saffron rich in crocin is consider as a pure saffron. Crocin act as an in-vivo Antioxidant and in-vitro Aphrodisiac activity. Safranal shows antitussive and Anticonvulsant activity.
To check the quality and purity of saffron many authors/researchers perform several experiments such as TLC, HPTLC, FTIR, UV/Visible spectroscopy etc.
Key words: - Crocus sativus, Aphrodisiac, safranal, crocin, HPTLC(High Performance Thin Layer Chromatography).

I. INTRODUCTION

Saffron is highly valued and most expensive spice because of its medicinal properties. It consists of stigma and tops of the styles of crocus sativus. 70% preparation is a process of making something conform to a standard. standardization of herbal drugs is necessary for the verification of drug is done in Spain and other are Kashmir and Iran [1].

The demand for saffron has been increased due to the production of various new products and the conditions of cultivation [2].

Saffron is known to have a very significant part of Siddha and Unani for last 3500 years. according to Spanish food coat saffron spice is defined as crocus sativus having maximum tolerance of styles and floral waste specified for various qualities in corresponding regulation. This plant grows on arid or semiarid lands adaptable to temperate and subtropical climate at an altitude ranging between 600 to 800m from sea level. This plant is widely grown in India in Jammu and Kashmir, Himachal Pradesh, and Uttarakhand [3].

The plant is utilized in traditional Persian medicine. Owing to its high price many times it is subjected to adulteration of various types. Hence qualitative and quantitative tests are performed to study its purity and quality [4].

Standardization is the process of setting quality parameters .it of its identity, quality, and purity. Many methods have been developed for standardization of herbal drugs such as physical, botanical, biological, chemical and chromatographic techniques. Chromatographic techniques include thin layer chromatography (TLC), high performance liquid chromatography (HPLC), high performance thin layer liquid chromatography (HPTLC) etc. [5] .

Standardization of saffron is carried out to check the quality and quantity of its chemical constituents by using various methods. Among the all methods HPTLC is the most superior [6].

II. PLANT PROFILE

Synonyms: Bhavarakta, Mangalya, Agnishikha, Kumkuma, Kashmirajanma , saffron, kesar, Safran and Jafran [7].
Geographical source: It is widely cultivated in India (Kashmir), Spain, France, and Greece [8].
Macroscopy:stigmas are dark red to reddish brown in color having strong, characteristic, and aromatic odour. stigmas are 25mm long in size and style about 10mm long [8].

Chemical constituents

Crocus consist of many chemical components in its stigma. sugar, minerals, fats and vitamins are primary constituents while terpenes, flavonoids, anthocyanins and carotenoids are secondary constituents. Between all these constituents'carotenoids are consider as the most important chemical constituent. Carotenoid determine the color and taste of crocus spice. Lipophilic and hydrophilic carotenoids such as æ ,ß carotene, lycopene and xanthine have been

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identified in trace amount.chief pigmnent of saffron is crocin approximately 80 % [4].
Saffron name is derived from Arabic word which means yellow color. The yellow color is due the presence of high concentration of carotenoid pigment in the saffron stigma [3]

Red coloring matter present in saffron are crocin and crocetine, picrocrocin imparts bitter taste to saffron. It also contains traces of volatile oil. protocrocin is a carotinoid glycoside [8]

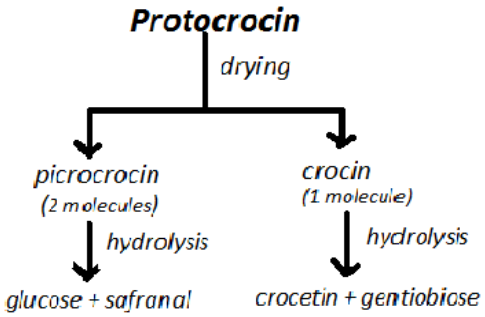

Fig 1: Flow chartofchemical constituents [8]

Crocin is a digentiobioside, its high solubility is due to the sugar moieties. It is deep red in color, dissolve quickly in water and form an orange-colored solution, hence it is widely used as natural food colorant [3].

Crocin is also called as polychroite [8]. Crocusatins A-E are the five new monoterpenoids are obtained from the pollens and crocusatins F-I from the stigma [1]

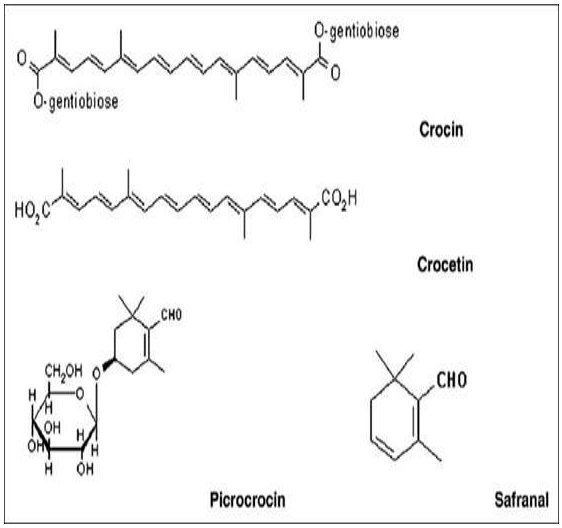

Fig 2: - Structure of Crocin, Crocetin, Safranal,Picrocrocin.

Uses : Saffron is used as colouring and flavouring agent . it is also used asantispasmodic,emmenagogue, stimulant [8],aphrodisiac and cosmetic industries [9]

Fig 3 : Saffron Flowers.

Fig 4 : Saffron Stigmas.

Fig 5 : Saffron Stigma Powder.

III. LITERATURE REVIEW:

There are many analytical methods are developed for separation and qualitative studies for saffron, such as uv-vis spectrophotometry, TLC and HPLC have been developed to analyze saffron.
Two different sample of saffron we from two different Himalayan region of India having different geographical and climatic conditions. Further the sample were named as S1 and S2 by the author [4] .

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I. Pharmacognostic review

Macroscopy

Dr. C.K. Kokate et al 2016studied macroscopic characteristic of saffron and found that stigmas are dark red to reddish brown in colorand style is yellowshish brown in color [8].

Microscopy

R. Srivastav et al 2008studied microscopic characteristic of saffron stigma using microscope. After observing soaked drug under microscope, the stigmas are discrete or joined in three to the apex of yellow style. Shape of stigma is slender funnel and the rim is dentate [10].

Stigmas are elongated, thin-walled parenchyma which contain coloring matter. At the distal end of stigma there are bladdery, club like papillae, among which occur a few smooth, spherical pollen grains. Calcium oxalate crystals are present [11].

II. Phytochemical review

S.K. Shukla et al 2015performed certain chemical test on saffron stigma. Phytochemical analysis Such as total ash value, Extractive value was carried out by the author as prescribed in Ayurvedic Pharmacopoeia of India and Preliminary tests were also carried out according to standard procedures and methods. Preliminary tests such as, Physical tests: texture and condition, color of the stigmas etc. Color test, Cotton color test,

Floatation test: genuine saffron floats on water.

Whatman paper test: adulterated saffron give yellow color more quickly.

after these tests they carried out the chemical examination which include reactions with,

Sulphuric acid (H2SO4showed indigo blue color.

Nitric acid (HNO3): light blue color.

Ammonia (NH3): yellow orange color etc. [12].

Both the sample (S1 & S2) were soaked and kept overnight in the solvent. Next day, these were boiled and filtered. both the filtrates S1 and S2 were concentrated in standard flask [4].

III. Analytical Review

After extraction research perform several analytical tests such as

1. TLC (Thin layer chromatography)

AK Mangal et al 2018carried out TLC by pre coated silica gel 60 F252 using solvent system which was selected by trail and error method. The Chromatograms were developed in glass chambers and both the plates were allowed to travel through the mobile phase up to 8cm from starting point and then the plates were sprayed with spray reagent (anisaldehyde-H2SO4). After the development, the plates were observed under the UV and recorded the Rf values. in this TLC study the researcher found that sample no.1 contains higher no of phytoconstituents as compare to sample no.2 [4] .

Rajaa A. Hussein et al 2018 TLC was performed on the chemical constituents of saffron extract. Analysis was done using aluminum-backed TLC (thin layer chromatography) plates, sample were developed in the mobile phase, butanol: acetic acid: water (4:1:1) v/v/v. under the uv light and visible light separated constituents were observed. With the help of TLC crocin was identified. Single separation spot of TLC chromatogram was displayed. It was having conjugated double bond which appears as fluorescent spot under UV-lamp with R_f value (0.7). the separation spot showed dark brown color in UV lamp and yellow in visible light [13].

2. HPTLC (High Performance Thin Layer Chromatography)

HPTLC is one of the modern instrumental techniques for qualitative and quantitative analysis of herbal drugs [6] .

AK MANGAL et al2018performed this HPTLC technique using the solvent system toluene: ethyl acetate: acetic acid (5:5:0.1) and the plates were dried and observed under the UV 254 and UV 366nm. Then the plates were deep in vanillin sulphuric acid reagent and heated in the hot air oven at 105°C. CAMAG HPTLC densitometer. Further the results such as Rf vale, color band and peak areas were noted.

HPTLC profile of sample 1 showed 10 peak and sample 2 showed 8 peaks [4].

3. FTIR (Fourier Transform Infrared spectroscopy)

Riyaz Ahamad et al 2011performed FTIR to detect the functional groups present in the chemical constituents of saffron. FTIR of crocin showed following functional groups (-CH=CH-) ,(-C-O-C- ether) ,(-C-O- ester) , (-C=C-) , (-C=O-),(-O-H) and (-C-H) [14].

Rajaa A. Hussein et al 2018 determined the functional present in the saffron with the help of FT-IR. FT-IR showed the single peak at 3415 cm^{-1} allied to vibrational stretching for -OH bond specified the presence of alcoholic group. The vibrational stretching of C-H bond of methyl group symmetrically and asymmetrically were related to bands at 2924 cm^{-1} and 2854 cm^{-1}.the bands at 1662 cm^{-1} indicated the presence of C=O bond of ester

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due the presence of carotenoid compound. It was confirmed that the isolated compound was crocin when it was compared with the standard crocin [13].

Adil Farooq wali et al 2020 performed the FTIR analysis of saffron petals extract. FTIR was performed on carry 630 FTIR spectrophotometer equipped with MicroLab software. The spectra were obtained at λ_{max} 4000 and 6000cm^{-1}, with resolution of 8cm^{-1}. Functional groups were identified at different bands are as follows,

C-H and CH_2 of aliphatic hydrocarbon at the band 2917.5cm^{-1},

C-H stretching of aldehyde at band 2849.75cm^{-1},

C=O stretching at band 1707.975cm^{-1},

C-H bending at band 1459cm^{-1},

C-O stretching of ester group at the band 1375.517cm^{-1},

C-O stretching of ester at band 1247.675cm^{-1},

O-H deformation at band 1034.127cm^{-1}[15].

4. UV VISIBLE SPECTROPHOTOMETRY

Mounira Lage et al determined the chief characters of saffron using UV-visible spectrophotometric method in which main constituents of saffron were analyzed. Picrocrocin, crocin and safranal are the main constituents of saffron. Higher the amount of these constituents higher is the quality of saffron. The result was obtained by direct reading of absorbance at three wavelengths, these are as follows:

257nm (maximum absorbance of picrocrocin),

330nm (maximum absorbance of safranal),

440nm (maximum absorbance of crocin).

Shimadzu U310 PC and UV-visible NIR scanning spectrophotometer these were the material used for the analysis [16].

Rajaa A. Husseinet al 2018performed the ultra-violet and visible spectroscopy on saffron extract. plant extract was dissolve in 80% ethanol (C_2HOH) to study the ultra violet in range of 200-600nm. Two peaks of UV spectrum were observed by the researcher one at λ_{max}314nm and another at λ_{max} 425 nm[13].

S . K. Shukla et al 2015 studied UV visible spectroscopy on the alcoholic extract of two samples, genuine and fake. In this analysis genuine sample showed absorbance 0.835 at wavelength 458.93 nm and fake saffron showed absorbance 0.159 at wavelength 432.42 nm [12].

F. Hadizadeh et al 2010 carried out UV- visible spectroscopy using a uv-1700 pharma spec system in the range of 200-600nm. Fluka crocin showed absorbance 2.37 at wavelength 440nm, saffron stigma extract showed absorbance 5.6 and crystalize crocin showed absorbance 13.4.

Order of UV absorbance: Fluka crocin ‹ saffron stigma ‹ crystallized crocin [17].

IV. Pharmacological review

1. Antiatherosclerotic effect:

XIN SU et al found the advantages of saffron on cardiovascular disease. Saffron was found to be an effective in many hearts' disease. it is used as antiatherosclerotic and Anti Ischemic [18].

2. Antiatherosclerotic :

Oxidative stress is the main cause of atherosclerosis. Overproduction of reactive oxygen species induces inflammation and associated with atherogenesis. In the in vitro study on bovine aortic endothelial cell crocin has shown decrease in the malondialdehyde levels at the dose range of (0.1, 1, and 10µmol/L). Crocetin also showed the same results as that of crocin.

In vitro study on rabbits crocetin showed antiatherosclerotic action. It was observed that crocetin reduces the level of malondialdehyde and inhibit the decrease of NO level inserum[18].

R.srivastava et al studied that when 50mg of saffron dissolved in 100ml of milk and was given BD (twice a day) to humans which results in significant decrease in lipoprotein oxidation in patient suffering from CAD (coronary artery disease). This shows the potential of antioxidant activity of saffron [10].

3. Antihypertensive effect

Vijaya Bhargava kreviewed the antihypertensive effect of saffron on laboratory animals. Ethanolic and aqueous extract of saffron petals shown decreased blood pressure in rats [19].

Zohreh Nasiri et al studied the antihypertensive effect of dietary saffron constituents (crocin and safranal) on male rats.28 male rats (180-220g) were taken for the experimental use. Using L-NAME (L-N-Nitro arginine methyl ester) 40mg/kg/day for 5 weeks hypertension was induced in male rats. Hypertension induction remarkably raised the systolic blood pressure from 123 to 176 mm Hg. Decrease in the blood pressure of rats was observed at the 3rd week of treatment. Dietary saffron antagonized the L-NAME induced raised in systolic blood pressure [20].

4. Antibacterial activity

Raja A. Hussein et al studied the antibacterial activity of saffron extract against selected bacteria at the concentration of 1000mcg/ml. Methanolic

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extract of crocin pigment exhibits highest antibacterial activity. Crocin showed antibacterial activity against all bacterial strain used (E.Coli and staphylococcus aureus) with the zone of inhibition ranges from 20-36mm[13].

5. Antioxidant activity

Raja A. Hussein et al evaluated the free radical scavenger activity of saffron. Methanolic extract of saffron stigma has showed antioxidant property. The antioxidant activity of saffron is due the presence of phenolic and flavonoid compounds [13].

Vijaya Bhargava k found that the crocin exhibits higher antioxidant capacity than vitamin E (alpha-tocopherol).it also increases the level of glutathione reductase, glutathione-S- transferase. crocin was found to maintain functional level of additional antioxidants [19].

Naveed Akhtar et al 2014evaluated the antioxidant activity of saffron. Antioxidant activity of saffronextract was determined with different solvents. The antioxidant activity ofsaffron extract using 70% of ethanol was 81% [21].

6. Anti-Alzheimer activity

Vijaya Bhargava k studied the anti-Alzheimer activity of saffron. The water: Methanol (50:50 v/v) extract of saffron stigmas inhibits the amyloid beta fibrillogenic [19].

Mohammad Saeedi et al reviewed anti-Alzheimer activity of saffron on animals. Animals study has shown effective action of saffron against Alzheimer disease. The main cause of Alzheimer disease is deposition of Aβ fibers in the brain. Water : Methanol (50:50) extract of saffron stigma has shown superior antioxidant property and inhibits Aβ fibrillogenic in a concentration . Administration of crocin orally 100mg/kg for twenty-one days can ameliorate STZ (streptozotocin)-induced spatial memory deficiency [22].

Nikolaos Pitsika 2015 studied effect of saffron on Alzheimer's disease. 46 patients with mild to moderate Alzheimer's disease were treated with 30mg of saffron extract or 10mg of donepezil per day in multicenter clinical trials. The result was obtained which showed that after 22 weeks saffron exhibits similar effect on Alzheimer's disease as that of donepezil [23].

7. Anti tussive activity:

Vijaya Bhargava k found thatEthanolic extract of saffron showed reduced in cough using guinea pig as a model nebulize solution of citric acid was used to induce the cough [19].

R.srivastavanalyzed the antitussive activity of saffron stigma and petal extract and its components crocin and safranal was estimated in guinea pigs using spray solution of citric acid 20%. Ethanolic extract of saffron 100 to 800mg per kg and safranal 0.25 to 0.75 mg per kg decreases the cough. Crocin did not show this antitussive activity [10].

8. Anticonvulsant action

Vijaya Bhargava k studied Safranal when administered peripherally to the rats was found to produce dose dependent decrease in generalize tonic clonic and minimal clonic seizures induced by pentylenetetrazol administration [19].

R.srivastavreviewed the anticonvulsant activity of saffron stigma constituents crocin and safranal. Anticonvulsant activity was estimated in mice using PTZ (pentylenetetrazol)-induced convulsion. Delay in onset of grand mal seizures, Reduced seizures duration, and protection of mice from death is due to safranal, when administered intra peritoneal in the dose range of 0.15 and 0.35ml per kg body weight. Anticonvulsant activity was not shown by crocin (22mg/kg IP.) [10].

9. Anti emollient and pruritic effect

R.Srivastavreviewed the anti-emmolient property of saffron. Topical formulation of saffron at the concentration of 0.025%v/w was found to have effective in atopic dermatitis, ichthyosis vulgaris and other skin infections [10].

10. Peptic ulcer

Alireza Rezaee et al 2016 reviewed the effect of ethanolic extract of saffron and omeprazole against gastric ulcer induced by indomethacin in non-diabetic and streptozocin diabetic rats. Saffron reduces the lipid peroxidation and improve the glutathione levels and prevents the damage of gastric mucosa. N-095 is a nutrient drug which possess antiulcer properties. This nutrient drug contains 90mg of saffron has shown ulcer protective action [24].

11. Effect of saffron on ocular blood flow and retinal function

Alireza rezaee et al 2016studied the effect of saffron on eye. Long term intake of saffron for 14 weeks 20mg/day has shown improvement in visual quality and macular function. Crocin improves the retinal function by increasing the blood flow to choroid and retinal [24].

12. Toxicity of saffron on cancer cell

Masihollahshakeri et al 2020 studied the toxicity of saffron on cancer cell.

International Journal of Pharmaceutical Research and Applications
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In vitro anticancer effect of saffron:

It was found that the tumor cells were more sensitive to ethanolic extractof saffron than normal cells. saffron extract has inhibitory effect on DNA andRNA synthesis. saffron extract at the concentration of 20, 40 and 100 microgram/ml applied for 24, 48, and 72hrs. reduced the expression self-renewalgenes such as OCT4 and KLF.

On rat model ethanolic extract of saffron had selective cytotoxic effecton epithelial cell like hepatocellular carcinoma, while it has no effect onnormal cells.

In-vivo anticancer effect of saffron:

Saffron extract delayed the emergency and progression of skin tumor in ratsby oral intake of saffron extract 100mg/kg body weight up to 12 weeks [25].

13. Antifungal activity of saffron

defu wang et al 2021studied the antifungal property of saffron. Ethyl acetate phase of saffronlateral bud ethanolic extract of saffron evoked a remarkable antifungal effectagainst tested fungi, especially Trichoderma viride (79%) and aspergillusniger (83.4%)[26].

14. Aphrodisiac activities

Arshad Husain et al 2017revealed the aphrodisiac property of saffron. Saffron increases libido in male and improve fertility when consumed. Aqueous extract of crocin at the doses of 160-320mg/kg b.w has increased mounting and erection frequency behaviors and reduced ejaculation, intromission, and mount latency parameters [27].

H. Hosseinzadeh et al 2008studied the aphrodisiac activity of saffron. Activity was revealed using rat model. Intraperitoneal administration of crocin at the dose range of (100,200 and 400ml/kg), Aqueous extract (80,160 and 320mg/kg), Safranal (0.1,0.2 and 0.4ml/kg), sildenafil (60mg/kg was positive control) and saline to male rats showed increase in mounting frequency, erection frequency and ejaculation latency[28].

IV. RESEARCH AREA: -

Thoughts

- Microscopic Characters can be studied.
- Extraction of Crocin From saffron by using extraction techniques: Super Critical Fluid extraction (SFE), Microwave-assisted extraction (MAE) and Vacuum-assisted extraction (VAE).
- NMR can be done to identify the structure of molecules.
- Adulterated and Pure drug identification.
- HPLC can be done to check quality control and Identity/Purity.
- Other Pharmacological activity can be evaluated using various animal model (rats, guinea pigs and rabbits) .

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