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A REVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL STUDIES OF *CROCUS SATIVUS* (SAFFRON) AND *TERMINALIA CHEBULA*

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ABSTRACT

The kingdom of plants has been shown to be the most successful in the treatment of many diseases, and it is a significant source of all medicines used globally. Alternative medicine is currently spreading over the world and getting more and more popular. Terpene alcohol, terpenes & esters make up the majority of the ingredients in saffron, but it also comprises over than 150 other volatile & aroma-producing substances. Antigenototoxic, antihypertensive, cytotoxic, anticonvulsant, and antitussive activities are among the medical benefits of the Iridaceae plant species Crocus sativus L. (syn. kesar). the Terminalia chebula family of the Combretaceae genus (also known as T. chebula). The amazing ability of Terminalia chebula to heal wounds and its wide variety of therapeutic properties have earned it the title of "King of Medicines" in Tibet.. In traditional medicine, it performs the function of a mild, secure, and efficient laxative. Aside from protecting the heart from harm, it is also used to treat kidney diseases. It also improves learning and memory while increasing blood flow to the choroid and retina. This review provides a high-level overview of the biology and pharmacological characteristics of numerous T. chebula and saffron extracts to further our understanding of these plants.

Key Words: Anticonvulsant, antinociceptive, Crocus sativus, safranal, Terminalia chebula; Triphala

1. Introduction

The dried, deep-red stigmas of the Iridaceae plant Crocus sativusL. are used to make saffron. The 85 species that make up the Crocus genus include saffron, which is perhaps an most fascinating and interesting species[1]. The name "saffron" is derived from the Arabic word za'faran, which means "yellow." The dried stigmas of the triploid sterile saffron flower are used to make commercial saffron, which is used in cooking and has a flavour and aroma that are highly potent and reminiscent of honey. On the origins and dissemination of saffron, there are numerous ideas. Some scientists disagree, but others think the saffron plant is native to Greece. The saffron crocus has the longest documented history when compared to other flowers[2]. Iranian medical writings provided a description of this common herb [3]. These days, this well-known plant is grown in many other regions of the world, including China, Turkey, Central Asia, and Europe[4-5]. The

chemical composition of saffron is composed of 63% of the ingredients are sugars, 12% are proteins, 10% are water, and 5% (%w/w) are crude fibre, fat, and minerals. Despite the fact that saffron stigmas contain over 150 volatile substances, crocin (C44H64O24), picrocrocin (C16H26O7), and safranal are the main bioactive components of this legendary herb (C10H14O).These substances give saffron its distinctive hue, flavour, and aroma, in that order [6]. Mineral agents, anthocyanins, glycosides, alkaloids, and specific flavonoids are all present in the saffron petal in addition to the substances that are found in this plant, such as quercetin and kaempferol [7]. Saffron's main bioactive ingredients are derived from carotenoids[8]. Persian traditional medicine use saffron as a treatment for depression. [9] Frequently, saffron pistils are used as analgesics, cardioprotective agents, and remedies for a variety of mental illnesses in traditional Indian medicine. The crude extract from saffron pistils improves memory and learning in rats and speeds their recovery from ischemia/reperfusion injury. Traditional medicine recommends the use of saffron as an aphrodisiac. [10].

The Combretaceae family member T. chebula can be found all over India, however it is more prevalent in deciduous woods and areas with low rainfall [11]. The medium to large deciduous tree T. chebula has broad, spreading branches, a disk-shaped crown, and a height of up to 30 metres[12]. T. chebula is referred to as harad in Hindi, but its common name in English is black myroblans. There are 250 species of Terminalia, which are found throughout the world's tropical regions[13]. Numerous folk healers respect the fruits of T. chebula.; Tibetans view it as the "king of medicines," and ayurvedic apothecaries rank it second to none. The Sanskrit word "ikatiraH" has several meanings; in addition to referring to the yellowish dye it contains (haritak), It also implies that the plant is capable of curing (harayet) all illnesses and that it grows in the Himalayan region, the birthplace of the Hindu god Siva. It is increasingly recognised as a key source of unique biologically active compounds used in the production of industrial products and the treatment of a broad range of illnesses [14].

Taxonomical classification

C. sativus		***Terminalia Chebula***	
Kingdom	Plantae	**Kingdom**:-	Plantae
Division:-	Magnoliophyta	**Division**	Magnoliophyta
Class:-	Liliopsida	**Class:-**	Magnolipsida
Order:-	Asparagales	**Order:-**	Myrtales
Family:-	Iridaceae	**Family:-**	*Combretaceae*
Genus:-	*Crocus*	**Genus**:-	*Terminalia*
Species:-	*C. sativus*	**Species:-**	*Chebula*

2. Chemical constituents

Chemical investigations of stigmas from Crocus sativus reveal that they include carotenoids such crocetin (also calledα- "crocetin" or "crocetin I") and Glucoside, gentiobioside, glucoside, and diglucoside are its glycosidic forms, along with digentiobioside (also known as "crocin"). γ- α-

Crocetin (monomethyl ester),γ-crocetin (dimethyl ester), and 13-cis crocetin are carotenoids (trans crocetin isomer), zeaxanthin, lycopene, and mangicrocin (a xanthone-carotenoid glycosidic conjugate)(Figure 1) [15]. Saffron gets its colour from a rare class of water-soluble carotenoids called as crocins (cis & trans glucosyl esters of crocetin). The monoterpene aldehydes picrocrocin and safranal (dehydrocyclocitral), which are their deglycosylated derivatives, were hydrolyzed during drying and storage. Vitamins, particularly thiamine and riboflavin, minerals, amino acids, proteins, carbohydrates, gums, and gum globules, as well as anthocyanins, flavonoids, and vitamins. Along with 5 to 8% fat and wax, 12 to 13% protein, and a few essential oils that help create the strong saffron scent, they are also included [16].

In T. chebula, 32% of the tannin is made up of tannin. The plant T. chebula includes 14 hydrolysable tannins, including the Casuarinin, 1,6-di-Ogalloyl-ß-D-glucose, 1,2,3,4,6-penta-Ogalloyl-ß-D-glucose, and 3,4,6-tri-Ogalloyl-ß-D-glucose are glycosides. Geological variation affects the concentration of tannin(Figure 2). Triterpenoids, such as coumarin conjugated to gallic acid termed as chebulin, flavonol glycosides, phenolic compounds, and other substances were found[12]. T. chebula fruit was also used to extract luteolin and ethyl gallate. In addition, it includes vitamins, minerals, and amino acids like vitamin C. [13].

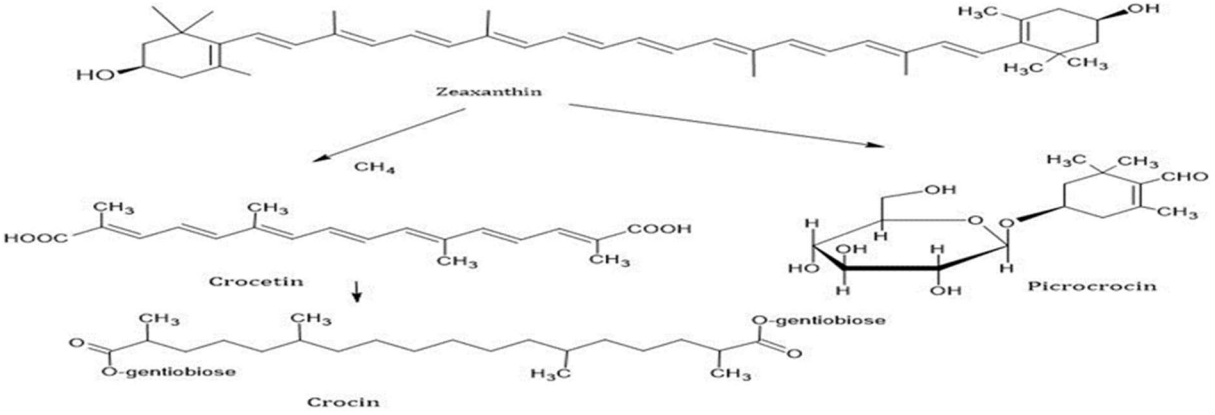

Fig 1.Saffron Constituents

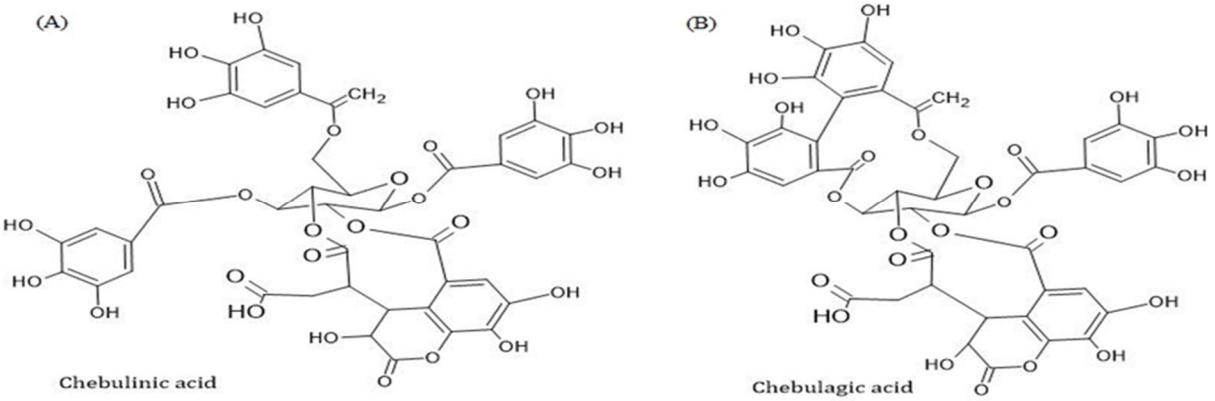

Fig 2. Structure of some phytoconstitutente T. chebula. (a)Chebulinic acid (b)Chebulagic acid.

3.Medicinal and pharmacological properties

3.1Sativus Crocus

3.1.1.Preventing Alzheimer's:

Trans-crocin-4, the digentibiosyl ester of crocetin, the main carotenoid, prevented the development of A-beta fibrillogenesis, which is brought on by the oxidation of amyloid beta-peptide fibrils. The water: methanol (50:50, v/v) extract of Crocus sativus stigmas inhibited A beta fibrillogenesis in a concentration- and time-dependent manner at lower concentrations than its other constituent, dimethylcrocetin [17].

3.1.2. Anti-Tussive qualities:

It was found that When a nebulized solution of citric acid (20%) was used to produce coughing in guinea pigs, an ethanolic extract of Crocus sativus and its component safranal reduced the number of coughs [18].

3.1.3. Reduction of cholesterol:

At doses between 25 mg/kg and 100 mg/kg , BW(Body Weight), crocin, a component of saffron, been discovered have lipid lowering effects on rats with diet-induced hyperlipidemia. This was accomplished by blocking pancreatic lipase, which causes a poor absorption of fat & cholesterol and has adverse effects on lipid levels [19].

3.1.4. Effect of an anticonvulsant :

After peripheral injection of pentylene tetrazole, it was shown that safranal, Saffron's colourant decreased the frequency of rats' generalised tonic-clonic seizures & moderate clonic seizures in a dose-dependent way. The capacity of safranal to function in this manner was thought to be at least partially mediated by the GABA (A) benzodiazepine receptor complex [20]. When mice were subjected to pentylenetetrazole, another component of saffron called crocin had no effect on the convulsions the mice experienced [21].

3.1.5. Antipruritic and emollient effects:

An effective treatment for ichthyosis vulgaris, atopic dermatitis, and other minor xerotic conditions was found to be with a 0.025% v/w concentration of crocus sativus in a topical application [22].

3.1.6. Anti-inflammatory and painkilling properties:

According to the results of the Saffron stigmas and petals exhibit immediate and sustained anti-nociceptive and anti-inflammatory effects, as shown by the writhing test, xylene-induced mouse ear oedema, and formaldehyde-induced rat paw oedema. This is in support of its long-standing use as a method of edoema prophylaxis.

3.1.7. Efficiency of antioxidants :

As a potential food supplement or cosmetic to treat age-related illnesses, Crocus sativus's methanolic extract and its ingredients, including safranal and crocin, have been proposed. [23]. In neuronally developed, glucose-depleted pheochromocytoma cells, crocin was discovered to be a more potent antioxidant than alphatocopherol. These cells' In the absence of glucose, the intercellular superoxide dismutase activity of cell membrane lipids reduced and they became peroxidized. Therefore, crocin proved its potential as a unique and effective antioxidant that shields neurons from oxidative damage. Additionally, it was said to maintain the functioning levels of other antioxidants while increasing the levels of a variety of enzymes, including glutathione S-transferase and glutathione reductase, indicating that it might be a trustworthy antioxidant.

3.1.8. Defence against genotoxicity:

The genotoxicity caused by medications including cisplatin, urethane, cyclophosphamide, and mitomycin C was lessened by the aqueous saffron extract in a mouse bone marrow micronucleus test. In addition, rats pretreated with saffron showed greater levels of liver enzymes including glutathione s-transferase.In addition, it was observed to decrease lipid peroxidation while increasing liver enzymes like non-enzymatic antioxidants, catalase, and superoxide dismutase,preventing the oxidative stress caused by these medications. This suggests that saffron's chemopreventive effects are mediated through modulation of lipid peroxide [24].

3.1.9. Crocus sativus alcohol extract reversed the suppression of Rats under anaesthesia have long-term potentiation in their dentate gyrus' hippocampus., indicating that it may be utilised to counteract the deleterious effects of ethanol and acetaldehyde, its major metabolite [25].

3.1.10. Cardioprotection:

Saffron's primary component, crocetin, was found to have a cardioprotective effect by decreasing the amount of the cardiac marker lactate dehydrogenase activity and raising mitochondrion potential in a cardiac myocyte that had been subjected to noradrenaline[26]. Further evidence of saffron's calcium-opposing effects was presented. This antagonistic activity was achieved by preventing the opening of Ca (2+) channels controlled by receptor to extracellular Ca (2+).Potential-dependent Ca (2+) channels. Crocetin inhibited the heart hypertrophy brought on by norepinephrine in a different study by boosting the levels of antioxidant enzymes such glutathione peroxidase, catalase, and myocardial superoxide dismutase. Additionally, it considerably lessened the norepinephrine-induced cardiac degenerative histological alterations [27].

3.1.11. Preventing the development of diabetes:

In rats fed fructose, the active component of saffron, crocetin, was discovered to exhibit anti-diabetic characteristics. In primary cultured rat adipocytes, It prevented the development of free fatty acid-induced insulin insensitivity and dysregulated the mRNA expression of adiponectin, TNF-alpha, and leptin, suggesting that crocetin therapy could be used as a strategy to prevent insulin resistance and associated diseases [28]. Advanced glycation end products are recognised to be the initiator of the oxidative process that usually causes endothelial cell loss and therefore diabetic vascular problems. Crocetin may be an effective remedy for diabetic vascular problems due to its high antioxidant capacity and calcium antagonistic activity or stability [29].

3.1.12. Respiratory infections:

As demonstrated in the guinea pig tracheal chain experiment, Crocus sativus has a relaxing effect on smooth muscle. When compared to saline, which served as a negative control, and theophylline, the relaxation brought about by the aqueous/ethanolic extract and safranal was comparable to or even greater, suggesting that it may be used to treat various respiratory problems like asthma and other similar conditions [30].

3.1.13. Effects on retinal function and ocular blood flow:

Analogs of crocin, which were derived from Crocus sativus, were discovered to aid the recovery of retinal function, improve the flow of blood toward retina & choroid through vasodilation, &

stop age-related macular degeneration, which causes ischemic retinopathy and blindness [31].

3.1.14. Parkinson's disease prevention:

The use of Crocus sativus in focal ischeamia is suggested by the pre-treatment of rats with crocetin, It prevented a model of middle cerebral artery blockage from losing enzyme function (acute cerebral ischemia). An injection of specific substances, such as 6 hydroxy dopamine, or reactive oxygen species can cause Parkinson's disease, a neurodegenerative disorder, is characterised by the loss of neurons in the substantia nigra.. Crocetin is an effective treatment for this crippling illness as evidenced by the fact that pre-crocetin-treated experimental rats had increased antioxidant enzyme properties and defence against the negative effects of 6-hydroxy dopamine [32].

3.1.15. Effect on memory and learning behavoiur:

Saffron extract was discovered to have an impact on experimental animals' learning and memory in behavioural and electrophysiological investigations. In mice, drinking has been shown to reduce learning behaviour and A kind of activity-dependent synaptic plasticity known as "hippocampus long-term potentiation" may be the basis for learning and memory. Saffron extract in aqueous form has been shown to improve these results. It was claimed that crocetin was to blame for these effects of saffron extract, however what is actually occurring is crocin (crocetin digentiobiose ester). Saffron extract or its bioactive components, crocetin and crocin, may be beneficial for the treatment of neurodegenerative illnesses linked to memory impairment [33]. Additionally, it has been shown that crocin reduces TNF-induced cell death, preventing the death of neurons caused by both internal and external apoptotic stimuli [34].

3.1.16. Influences of Blood Pressure:

As well as in isolated rat vas deferens, guinea pig ileum, and other tissues where responses were elicited by electrical stimulation, the aqueous and ethanolic extracts of Crocus sativus petals caused a reduction in blood pressure in rats under anaesthesia in a dose-dependent manner. It was believed that postsynaptic mechanisms were responsible for this drop in blood pressure [35].

3.1.17. The impact of an antidepressant:

In a double-blind, randomised, placebo-controlled research that lasted six weeks, as well as in animal-based pre-clinical studies, The alcoholic extracts of the stigmas and petals of Crocus sativus have been shown to have antidepressive effects. This antidepressant activity was comparable to that achieved by the frequently prescribed medications fluoxetine and imipramine. [36].

3.1.18. The uterus's effects:

In conventional medicine, the plant is utilised to manage and regulate menstrual cycles. The back discomfort related to menstruation is also reduced by it. Hysteria and leucorrhoea are just a couple of the disorders that saffron can aid with. It can also be used to treat other female-specific ailments. For painful uterine issues, saffron pessaries were used [37]. Saffron was part of a polyherbal formulation that was demonstrated to elicit uterine contractions in rats when given at levels of 1000 and 2000 mg/kg [38].

3.1.19. Cancer and tumor-fighting activity:

When Swiss albino mice were transplanted with Ehrlich ascites carcinoma, Dalton's lymphoma ascites tumours, sarcoma 180 cells, or other tumours, the ethanol extracts of Crocus sativus increased the mice's survival time. Saffron and the T cell mitogen phytohemagglutinin were mixed in vitro and resulted in a non-specific proliferation of T cells. This demonstrates that the immune system may play a role in how well saffron combats tumours .Crocetin's potential as an anticancer drug was demonstrated in studies on lung cancer patients where it was discovered to lower lipid peroxidation, glutathione metabolising enzymes, as well as reverse the histological changes linked to tumour incidence [39]. It was discovered that crocetin marginally prevented the growth of skin tumours when mice were fed croton oil, 9, 10, dimethyl 1, 2, benzanthracene, 7, dimethyl benz, anthracin, and [40].By shielding rats against hepatocarcinogenic agents like dimethylnitrosamine and aflatoxin B1, crocins greatly decreased chronic liver damage in the rats. Studies on mice demonstrate that the hormone 12-O-tetradecanoylphorbol-13 acetate's capacity to promote the establishment of skin tumours is strongly inhibited by crocetin [41].In mice exposed to the skin cancer-causing compound 7,12-dimethylbenz[a]anthracene, topical treatment of saffron extracts delayed the development of papillomas and reduced the average number of papillomas per mouse. The increase in serum levels of ß-carotene and vitamin A in the experimental animals that received saffron was assumed to be the cause of the spice's anticancer effects. The research showed that crocetin had a dose-dependent inhibitory effect on the synthesis of DNA, proteins, and RNA in these human malignant cells, but it had no deadly effect on the colony formation of different tumour cells. It has also been demonstrated that a novel glucoconjugate made from the corms and callus of saffron has cytotoxic effects on a range of tumour cells from breast cancer, cervical epithelioid carcinoma, and fibrosarcoma [42].

3.2. Terminalia Chebula

3.2.1. Resistance of bacteria:

Several bacterial species resisted Terminalia chebula's antimicrobial effects. The common bacterium Helicobactor pyroli (H. pyroli), which has been linked to the emergence of stomach cancer, ulcers, and gastritis, has been successfully avoided using this method. Methicillin-resistant Gallic acid, which was extracted from an ethanolic extract of Terminalia chebula, and its ethyl ester failed to kill Staphylococcus aureus. Additionally, it has been discovered that Human pathogenic Gram (+) and Gram (-) bacteria are resistant to Terminalia chebula's antibacterial effects. Considering that T. chebula extract stopped germs from growing, Xanthomonas Campestris pv. strain XC-100. Citro demonstrates that the disease of citrus canker is successfully treated. The growth of intestinal bacteria, particularly Salmonella typhi, is also inhibited by it [43].

3.2.2. Antifungal properties:

The dermatophytes Trichophyton rubrum, Microsporum gypseum, Floccosum, and Epidermophyton, as well as the pathogenic yeast Candida albicans, are all susceptible to an application of Terminalia chebula's aqueous extract. Furthermore, it inhibited three yeasts (Candida spp.) and three dermatophytes (Trichophyton spp. [44].

3.2.3. Anti-viral behavior:

Gallic acid and three galloy glucoses were identified from the fruit of the T.chebula plant. The

galloyl moiety is essential for the compounds' ability to inhibit HIV-1 integrase's 3'-processing. Terminalia chebula has a long history of use for accelerating recovery from acute respiratory infections because to its retroviral reverse transcriptase inhibitory action, which safeguards epithelial cells from the influenza A virus. The functions of the immunodeficiency virus-1 transcriptase were also shown to be significantly inhibited by it [45].The effectiveness of Terminalia chebula in treating the Herpes Simplex Virus has been established in both animal and human studies (HSV).vivo and in vitro research. These findings inspired a team of Japanese scientists to investigate how T.chebula affect human cytomagalovirus (CMV). They got to the conclusion that T. chebula would be helpful for the prevention of CMV diseases in immunocompromised humans after learning that it was effective in stopping the multiplication of human cytomagalovirus in vitro and in an AIDS model using immunosuppressed animals. Additionally, it aids in the treatment of STDs and AIDS [46].

3.2.4.Qualities that are anti-mutagenic and anti-cancer:

The three phenolics of T.chebula that were shown to be the most growth-inhibitory were tannic acid, ellagic acid, and chelinic acid. According to studies on the inhibition of cancer cell proliferation by phenolics. Salmonella typhimurium has been demonstrated to be resistant to mutation by hydrolyzable tannins from Terminalia chebula.. Additionally, acetone extract from Terminalia chebula's bark and fruit powder contains elements that have potential antimutagenic/anticarcinogenic effect [47].

3.2.5. Anti-oxidant role:

Different levels of antioxidant activity were seen in four parts and six extracts from the Terminalia chebula fruit. On rats, it has been demonstrated that its fruit has antioxidant and radioprotective properties. The tert-butyl hydroperoxide (t-BHP)-induced oxidative damage exhibited in cultured rat primary hepatocytes and rat liver has also been demonstrated to be mitigated by an aqueous extract of the Terminalia chebula fruit[48].The main phenolic components were identified by HPLC using diode array detection as hydroxybenzoic acid derivatives, hydroxycinnamic acid derivatives, flavonol aglycones, and their glycosides; they had greater antioxidant activity than alpha-tocopherol [49].

3.2.6. Effects that are anti-anaphylactic and adaptogenic:

One of the 6 Ayurvedic plants whose adaptogenic potential was tested by feeding it to animals was Terminalia chebula fruit. Additionally, investigations on animals suggest that the plant's potent antianaphylactic effectiveness was demonstrated when blood histamine levels decreased after Terminalia chebula extract administration during the induction of anaphylactic shock. The animals were protected against a variety of stresses by the six traditional rasayana herbs, each of which worked in a distinctive manner [50].

3.2.7. Activity that lowers lipids and cholesterol:

Experimentally produced atherosclerosis has been proven to be resistant to Terminalia chebula extract's hypolipidemic effect. It also exhibited a hypocholesterelomic effect on rabbit atherosclerosis and hypercholesterolemia induced on by cholesterol [51].

3.2.8. Improving gastrointestinal movement and anti-ulcerogenic activity:

Despite having a long history of use as a laxative, research has revealed that the Terminalia chebula fruit can hasten stomach emptying. It was discovered that the increased secretory activity of the Brunner's gland was matched by a protective effect on the gastrointestinal mucosa, preventing duodenal ulcers [52].Rifampicin (RIF), isoniazid (INH), and pyrazinamide (PZA) were administered to mice, resulting in hepatotoxicity that was later found to be attenuated by Terminalia chebula extract. subchronic model [53].

3.2.9. Cardiovascular protection:

In rats with isoproterenol-induced heart damage, pretreatment with an extract from Terminalia chebula reduced the drug's effects on the generation of lipid peroxide while keeping the activity of the diagnostic marker enzymes. An isolated frog heart model has shown its pericap to provide cardioprotective advantages [54].

3.2.10. Cell-protective function:

The extract contained gallic acid (GA) and chebulic acid (CA), which are the active components of the herbal medicine Kashi (myrobalan, the fruit of Terminalia chebula). This prevented cytotoxic T lymphocytes (CTLs) from causing cytotoxicity. The exocytosis of granules in response to anti-CD3 stimulation was also reduced by the same dosages of GA and CA.The fruit extract of Terminalia chebula that contains ethanol significantly reduced cytotoxicity in HEK-N/F cells. Additionally, the extract's cytoprotective effects against UVB-induced oxidative damage were notable. The results were caused by the Terminalia chebula extract's inhibition of the age-dependent shortening of the telomere length, as shown by Southern blots of DNA extracted from sub-culture passages (TRFs). It appeared to have cytoprotective effects on gastric mucosa in vivo and had symptoms of the development of duodenal ulcers. Additionally, studies on its fruits have demonstrated that they have cytoprotective effects against oxidative stress and an anti-aging effect on cells [55].

When Terminalia chebula extract was administered to the mice before their entire bodies were exposed to radiation, radiation-induced In the mouse liver, DNA oxidative damage and membrane lipid peroxidation were reduced. When human cells' DNA was exposed in vitro, it also protected them from being harmed by gamma radiation [56].

3.2.11. Retinoprotective and anti-diabetic properties:

In both short- and long-term studies using streptozotocin-induced diabetic mice, the fruit of the Terminalia chebula plant significantly decreased blood glucose levels and exhibited retinoprotective effects [57].

3.2.12. Effects of spasmolysis:

In one of the numerous investigations on Terminalia chebula, abnormal blood pressure and intestinal spasms were reduced to show the herb's "anti-vata" or "anti-spasmodic" characteristics. This demonstrates its continued value for gastrointestinal diseases like the spastic colon [58].

3.2.12. Healing of wounds:

It was revealed that the treated wounds healed more quickly when rats were given a topical using a leaf extract from Terminalia chebula that has been alcoholic.A faster rate of epithelialization and improved contraction rates are signs.Regulatory of the immune system In mice, Acute delayed

type hypersensitivity and humoral antibody (HA) titer were increased by Terminalia chebula aqueous extract (DTH).detrimental quality A Terminalia chebula oil fraction has been described as having purgative activity [59].

3.2.13. Bactericidal action:

In an experiment on hamsters with an amoebic liver abscess, Maximum cure rates for Terminalialia chebula and four more plants—Boerhavia diffusa, Berberis aristata, Tinospora cordifolia, and Zingiber officinale—were 73% and 89%, respectively, in the same experiment on mice with an experimental caecal amebiasis. [60].

3.2.14. Chemical preventative measures:

Male Wistar rats exposed to Terminalia chebula had chemopreventive effects on renal oxidative stress, toxicity, and cell proliferation response [60].

4. Conclusion

Saffron is the most expensive medicinal food item due to its importance in the long-term development of the locations where it is farmed. Made from the dried stigmas of the Crocus sativus (Iridaceae) plant, saffron is a well-known spice. It is also used in the pharmaceutical, cosmetic, and textile colouring industries. Many medicinal compositions contained the well-known stigmas. Saffron has recently attracted new attention due to its possible application in cosmetics due to its anti-aging, anti-sun, and anti-pigmentation characteristics. It can also be used as a pigment or in perfumes. With a wide spectrum of pharmacological and therapeutic qualities, T. chebula is one of the most versatile plants. This versatile plant is an important source of many different kinds of compounds with a wide variety of chemical structures. T. chebula possesses a number of pharmacological properties, but also contains a number of bioactive substances that make it beneficial against a wide range of disorders.

5. Acknowledgement

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6. References

1. Hosseinzadeh H, Nassiri-Asl M. 2013. Avicenna's (Ibn Sina) the canon of medicine and saffron (Crocus sativus): a review. Phytotherapy Research, 27(4): 475-483.
2. Nadkarni K. 1976. Crocus sativus, Nigella sativa. Indian materiamedica, (editor: K.M. Nadkarni), Popular Prakashan, Bombay: 386-411.
3. Mollazadeh H, Emami S A, Hosseinzadeh H. 2015. Razi’s Al-Hawi and saffron (Crocus sativus): a review. Iranian journal of basic medical sciences, 18(12): 1153.
4. Hoshyar R, Mollaei H. 2017. A comprehensive review on anticancer mechanisms of the main carotenoid of saffron, crocin. Journal of Pharmacy and Pharmacology, 69(11): 1419-1427.
5. Amin B, Hosseinzadeh H. 2015. Analgesic and anti-inflammatory effects of Crocus sativus L.(saffron). In Bioactive nutraceuticals and dietary supplements in neurological and brain disease Academic Press: 319-324.

6. Rezaee R, Hosseinzadeh H. 2013. Safranal: from an aromatic natural product to a rewarding pharmacological agent. Iranian journal of basic medical sciences, 16(1): 12.
7. Kubo I, Kinst-Hori I. 1999. Flavonols from saffron flower: tyrosinase inhibitory activity and inhibition mechanism. .J.Agric Food Chem, 47(10):4121-4125.
8. Poma A, Fontecchio G, Carlucci G, Chichiricco G. 2012. Anti-inflammatory properties of drugs from saffron crocus. Anti-Inflammatory & Anti-Allergy Agents in Med Chem (Formerly Current Medicinal Chemistry-Anti-Inflammatory and Anti-Allergy Agents), 11(1) :37-51.
9. Karimi G, Hosseinzadeh H, Khaleghpanah P. 2001. Study of antidepresant effect of aqueous and ethanolic extract ofCrocus sativusin mice. Iran J Basic Med Sci,4:11-15.
10. Madan C L, Kapur B M, Gupta U S. 1966. Saffron. Econ Bot, 20(4): 377-385.
11. Naik G H, Priyadarsini K I, Naik D B, Gangabhagirathi R, Mohan H. (2004). Studies on the aqueous extract of Terminalia chebula as a potent antioxidant and a probable radioprotector. Photomed. 11(6): 530-538.
12. Chattopadhyay RR, Bhattacharyya SK. 2007. Plant Review Terminalia chebula. Pharmacognos. Rev. 23:145-150.
13. Saleem A, Husheem M, Härkönen P, Pihlaja K. 2002. Inhibition of cancer cell growth by crude extract and the phenolics of Terminalia chebularetz. fruit. J. Ethnopharmacol., 81(3):327-336.
14. Karel DK, Ammar S, Jari S, Marja K, Jyrki L, Peteri T, Kalevi P. 2004. The Structural and Conformational analyses and antioxidant activities of Chebulinic acid and its thrice-hydrolyzed derivative,2,4-chebuloyl-ß-d-glucopyranoside,isolated from the fruit of Terminalia chebula. ARKIVOC. 7:83-105.
15. Cicero A F, Colletti A. 2021. Nutraceutical approach to age-related diseases—The clinical evidence on cognitive decline, In Human Aging Academic Press, 255-272.
16. Hosseinzadeh H, Younesi H M. 2002. Antinociceptive and anti-inflammatory effects of Crocus sativus L. stigma and petal extracts in mice. BMC pharmacology, 2(1), 1-8.
17. Zarghami N S, Heinz D E. 1971. Monoterpene aldehydes and isophorone-related compounds of saffron. Phytochemistry, 10(11): 2755-2761.
18. “Saffron” http://www.saffron.de/en/safron-chemicalstructure/ saffron.htm
19. Papandreou M A, Kanakis CD, Polissiou M G, Efthimiopoulos S, Cordopatis P, Margarity M, Lamari F N. 2006. Inhibitory activity on amyloid-β aggregation and antioxidant properties of Crocus sativus stigmas extract and its crocin constituents. J Agric Food Chem. 54(23): 8762-8768.
20. Hosseinzadeh H, Ghenaati J. 2006. Evaluation of the antitussive effect of stigma and petals of saffron (Crocus sativus) and its components, safranal and crocin in guinea pigs. Fitoterapia, 77(6): 446–448.
21. Sheng L, Qian Z, Zheng S, Xi L. 2006. Mechanism of hypolipidemic effect of crocin in rats: crocin inhibits pancreatic lipase. Eur J Pharmacol. 543(1-3): 116-122.
22. Hosseinzadeh H, Talebzadeh F. 2005. Anticonvulsant evaluation of safranal and crocin from Crocus sativus in mice. Fitoterapia, 76(7-8): 722–724.
23. Hosseinzadeh H, Sadeghnia H R. 2007. Protective effect of safranal on pentylenetetrazol-

induced seizures in the rat: involvement of GABAergic and opioids systems. Phytomedicine, 14(4): 256-262.
24. Chatterjee S, Datta R N, Bhattacharyya D, Bandopadhyay SK. 2005. Emollient and antipruritic effect of Itch cream in dermatological disorders: A randomized controlled trial. Ind. J Pharmacol., 37(4): 253-254.
25. Assimopoulou A N, Sinakos Z, Papageorgiou V. 2005. Radical scavenging activity of Crocus sativus L. extract and its bioactive constituents. PhytotherRes. : An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives, 19(11): 997-1000.
26. Premkumar K, Abraham S K, Santhiya S T, Gopinath P M, Ramesh A. 2001. Inhibition of genotoxicity by saffron (Crocus sativus L.) in mice. Drug ChemToxicol. 24(4): 421-428.
27. Shen X C, Qian Z Y, Chen Q, Wang Y J. 2004. Protective effect of crocetin on primary culture of cardiac myocyte treated with noradrenaline in vitro. Yao XueXueBao.=ActaPharmaceuticaSinica, 39(10): 787-791.
28. Liu N, Yang Y, Mo S, Liao J, Jin J. 2005. Calcium antagonistic effects of Chinese crude drugs: Preliminary investigation and evaluation by 45Ca. ApplRadiatIsot. 2005 Aug; 63(2): 151-155.
29. Shen X C, Qian Z Y. 2006. Effects of crocetin on antioxidant enzymatic activities in cardiac hypertrophy induced by norepinephrine in rats. Die Pharmazie-An International Journal of Pharmaceutical Sciences, 61(4): 348-352.
30. Xiang M, Yang M, Zhou C, Liu J, Li W, Qian Z. 2006. Crocetin prevents AGEs-induced vascular endothelial cell apoptosis. Pharmacological research, 54(4): 268-274.
31. Boskabady M H, Khazdair MR, Memarzia A, Ghasemi SZ. 2022. Herbal immunomodulators. In Herbal Biomolecules in Healthcare Applications, Academic Press, 551-572.
32. Xuan B O, ZHOU Y H, Li N A, MIN Z D, CHIOU G C. 1999. Effects of crocin analogs on ocular blood flow and retinal function. J OculPharmacolTher. 15(2): 143-152.
33. Saleem S, Ahmad M, Ahmad AS, Yousuf S, Ansari MA, Khan MB, Ishrat T and Islam F. 2006. Effect of saffron (Crocus sativus) on neurobehavioral and neurochemical changes in cerebral ischemia in rats. Journal of Medicinal Food. 9(2): 246 - 253.
34. Ahmad A S, Ansari M A, Ahmad M, Saleem S, Yousuf S, Hoda M N, Islam F. 2005. Neuroprotection by crocetin in a hemi-parkinsonian rat model. PharmacolBiochemBehav. 81(4): 805-813.
35. Mohebbati R, Kamkar-Del Y, Shafei M N, Rakhshandeh H, Aghaei A. 2021. Effects of hydroalcoholic extract of saffron petal on blood pressure and heart rate in hypertension induced by angiotensin II and L-NAME in anesthetized rats. Vet Res Forum. 2021 Spring;12(2):185-190. doi: 10.30466/vrf.2019.103224.2456. Epub 2021 Jun 15.
36. Noorbala A A, Akhondzadeh S H, Tahmacebi-Pour N, Jamshidi A H. 2005. Hydro-alcoholic extract of Crocus sativus L. versus fluoxetine in the treatment of mild to moderate depression: a double-blind, randomized pilot trial. J Ethnopharmacol. 97(2): 281-284.

37. Basti A A, Moshiri E, Noorbala A A, Jamshidi A H, Abbasi S H, Akhondzadeh S. 2007. Comparison of petal of Crocus sativus L. and fluoxetine in the treatment of depressed outpatients: a pilot double-blind randomized trial. Prog Neuro-psychopharmacolBiol Psychiatry. 31(2): 439-442.
38. Akhondzadeh S, Fallah-Pour H, Afkham K, Jamshidi A H, Khalighi-Cigaroudi F. 2004. Comparison of Crocus sativus L. and imipramine in the treatment of mild to moderate depression: a pilot double-blind randomized trial [ISRCTN45683816]. BMC Complement Altern Med. 4(1): 1-5.
39. Bhargava V. 2011. Medicinal uses and pharmacological properties of Crocus sativus Linn (Saffron). Int J Pharm PharmSci, 3(Suppl 3): 22-26.
40. Nair S C, Kurumboor S K, Hasegawa J H. 1995. Saffron chemoprevention in biology and medicine: a review. Cancer Biother.&Radiopharmaceuticals,. 10(4): 257-264.
41. Magesh V, Singh J P V, Selvendiran K, Ekambaram G,Sakthisekaran D. 2006. Antitumour activity of crocetin in accordance to tumor incidence, antioxidant status, drug metabolizing enzymes and histopathological studies. Mol Cell Biochem, 287 (1-2): 127-135.
42. Das I, Chakrabarty R N, Das S. 2004. Saffron can prevent chemically induced skin carcinogenesis in Swiss albino mice. Asian Pac J Cancer Prev, 5 (1): 70-76.
43. Kim H G, Cho J H, Jeong E Y, Lim J H, Lee S H, Lee H S. 2006. Growth-inhibiting activity of active component isolated from Terminalia chebula fruits against intestinal bacteria. J. Food Prot.69(9) : 2205-2209.
44. Mehmood Z, Ahmad I, Mohammad F, Ahmad S. 1999. Indian medicinal plants: a potential source for anticandidal drugs. Pharmaceutical Biology, 37(3): 237-242.
45. El-Mekkawy S, Meselhy M R, Kusumoto I T, Kadota S, Hattori M, Namba T. 1995. Inhibitory effects of egyptian folk medicines oh human immunodeficiency virus (HIV) reverse transcriptase. Chem. Pharmaceut. Bull., 43(4): 641-648.
46. Vermani K, Garg S. 2002. Herbal medicines for sexually transmitted diseases and AIDS. Journal of ethnopharmacology, 80(1): 49-66.
47. Lee H S, Jung S H, Yun B S, Lee K W. 2007. Isolation of chebulic acid from Terminalia chebula Retz. and its antioxidant effect in isolated rat hepatocytes. .Arch.Toxicol. 81(3) : 211-218.
48. Saleem A, Ahotupa M,Pihlaja K. 2001. Total phenolics concentration and antioxidant potential of extracts of medicinal plants of Pakistan. Z. Naturforsch[C], 56(11-12): 973-978.
49. Shin T Y, Jeong H J, Kim D K, Kim S H, Lee J K, Chae B S,Lee Y M. 2001. Inhibitory action of water soluble fraction of Terminalia chebula on systemic and local anaphylaxis. J. Ethnopharmacol. 74(2): 133-140.
50. Thakur C P, Thakur B, Singh S, Sinha P K, Sinha S K. 1988. The Ayurvedic medicines Haritaki, Amla and Bahira reduce cholesterol-induced atherosclerosis in rabbits. Int. J Cardiol., 21(2): 167-175.
51. Nadar T S, Pillai M M. 1989. Effect of ayurvedic medicines on beta-glucuronidase activity of Brunner's glands during recovery from cysteamine induced duodenal ulcers in rats. Indian J Exp. Biol., 27(11): 959-962.

52. Tasduq S A, Singh K, Satti N K, Gupta D K, Suri K A, Johri R K. 2006. Terminalia chebula (fruit) prevents liver toxicity caused by sub-chronic administration of rifampicin, isoniazid and pyrazinamide in combination. Human & exp. Toxicol., 25(3): 111-118.
53. Reddy V R C, Kumari S R, Reddy B M, Azeem M A, Prabhakar M C, Rao A A. (1990). Cardiotonic activity of the fruits of Terminalia chebula. Fitoterapia, 41(6): 517-525.
54. Chattopadhyay R R, Bhattacharyya S K. 2007. PHCOG REV: Plant Review. Terminalia chebula: An update. Pharmacognosy Reviews.1: 151- 157.
55. Gandhi N M, Nair CK K. 2005. Radiation protection by Terminalia chebula: some mechanistic aspects. Molecular and Cellular Biochemistry, 277(1), 43-48.
56. Gupta A, Kumar R, Pandey A K. 2020. Antioxidant and antidiabetic activities of Terminalia bellirica fruit in alloxan induced diabetic rats. South Afri. J Bot., 130: 308-315.
57. TriphalaHerbal Colon Cleansing, Constipation, Internal cleanser. AvailbleIn :http://www.ayurvediccure.com/triphala.htm.
58. Shivaprasad H N, Kharya M D, Rana A C, Mohan S. 2006. Preliminary Immunomodulatory Activities of the Aqueous Extract of Terminalia chebula. Pharmaceut. Biol., 44(1): 32-34.
59. Sohni YR, Kaimal P, Bhatt R M. 1995. The antiamoebic effect of a crude drug formulation of herbal extracts against Entamoebahistolytica in vitro and in vivo. Jethnopharmacol., 45(1): 43-52.
60. Prasad L, Khan TH, Jahangir T, Sultana S. 2006. Chemomodulatory effects of Terminalia chebula against nickel chloride induced oxidative stress and tumor promotion response in male Wistar rats. J Trace Elem. Med. and Biol., 20(4): 233-239.