

COMPUESTOS BIOACTIVOS DE INTERÉS EN EL AZAFRÁN DE LA MANCHA

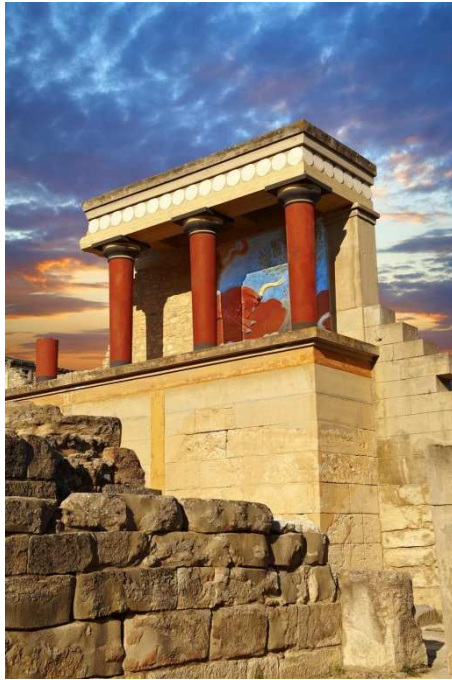


Dr. José Miguel Soriano del Castillo



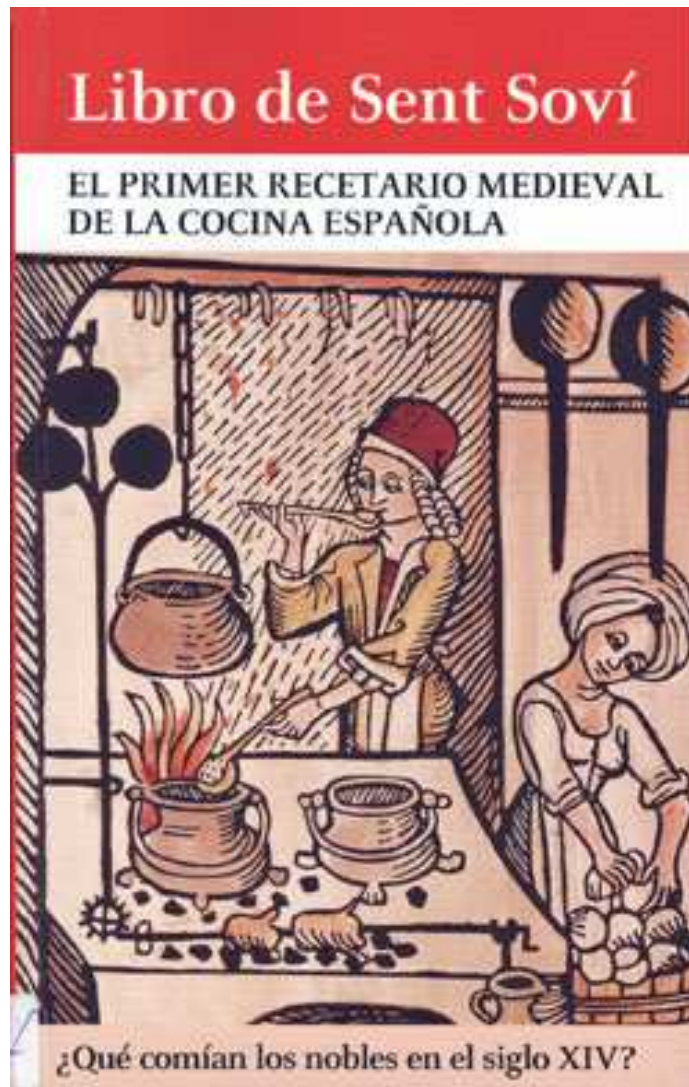
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Papiro de Ebers





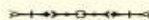
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FRANCISCO ABAD ALEGRÍA
de la Academia Aragonesa de Gastronomía



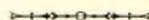
Discurso de ingreso



COLOR ROJIZO EN NUESTRA HISTORIA CULINARIA

El especiado con azafrán y pimentón
en las cocinas hispanas

19 de diciembre de 2001



Discurso de contestación
del Académico José M^a Pisa Villarroya



INSTITUCIÓN «FERNANDO EL CATÓLICO»
Excmo. Diputación de Zaragoza

AZAFRÁN

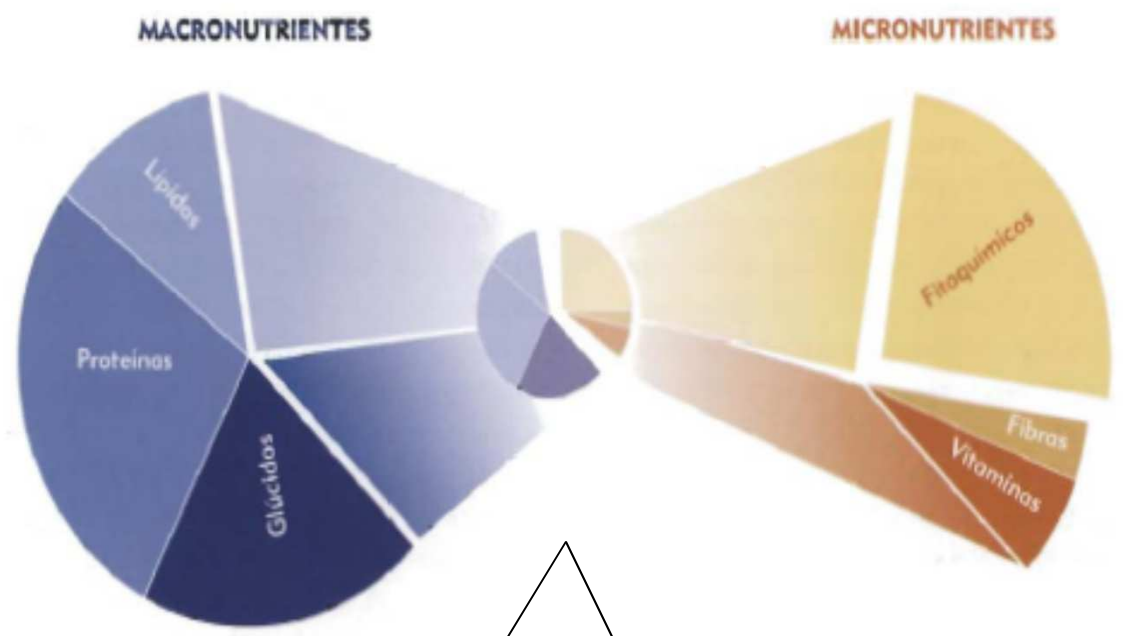
El azafrán sale de los estigmas del *Crocus sativus*, una planta liliácea oriunda de la zona griega y mediorientada. Su nombre deriva de la palabra árabe *az-zafran*, que designa al color amarillo oscuro; dependiendo de la concentración empleada, el color prestado a la comida o los tejidos (uso antiguo y no desdeñable del azafrán) varía entre el amarillo claro y el rojizo-pardo. Existen otras especies de azafrán, no comestibles. Es la especia más cara del mundo, en razón de la gran cantidad de materia prima precisa para obtener un peso apreciable de ella. No menos de 150.000 flores son necesarias para lograr un kilogramo de estigmas secos. Al tiempo, como pequeñas cantidades son suficientes para los trabajos culinarios, el precio resultante no es tan elevado.

Los medievales no concebían que sin azafrán se pudieran hacer buenos guisados. Es de compleción caliente entre el primero y el segundo grado. Es calefactivo, resolutivo, confortativo y aperitivo de las opilaciones de hígado y sobre todo es cordial.

Además del empleo culinario, del que oportunamente se hablará, se ha mencionado la utilización del azafrán como tinte, acreditado desde antiguo para la piel de los recién casados mesopotámicos y para las ropas de los hombres religiosos del Tibet. Pero también tiene otros usos que merecen comentario. Como especia llamativa por su color y aroma, no pudo pasar desapercibida para el mundo de la farmacia antigua. Es mencionado en el papiro de Ebers (s. XV a.C.) como remedio especialmente útil en enfermedades renales. Pero ya se hacía uso de él en el mismo Egipto, quince siglos antes; en estados febriles. También se encuentra formando parte de las fórmulas magistrales del embalsamamiento. En la Roma clásica, se prescribía como analgésico, antiinflamatorio, depurador hepatobiliar y para el tratamiento de abscesos y úlceras tórpidas. En *al-Andalus* sigue teniendo gran predicamento terapéutico, que sigue en la Edad Media. La revisión de algunos repertorios médicos, parece indicar que se utilizó en algunos casos que ahora se identificarían como cánceres.

En la medicina actual convencional, el azafrán no se emplea, aunque está aceptada una cierta acción antiviral y de control de las cifras elevadas de colesterol en sangre.

COMPOSICIÓN MOLECULAR DE LOS ALIMENTOS

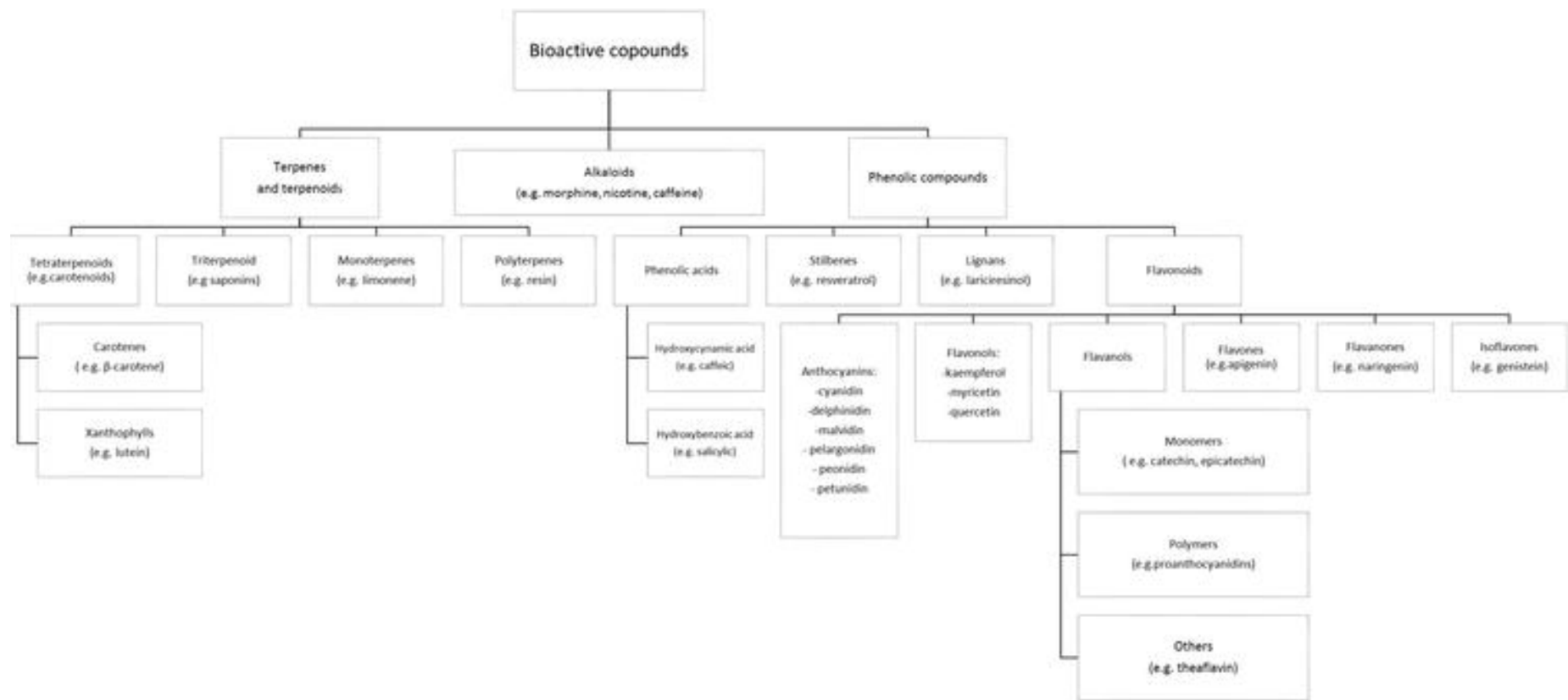


Extracto alimentario

Componente biológicamente activo de los alimentos/nutrientes

Individual

Colectivo



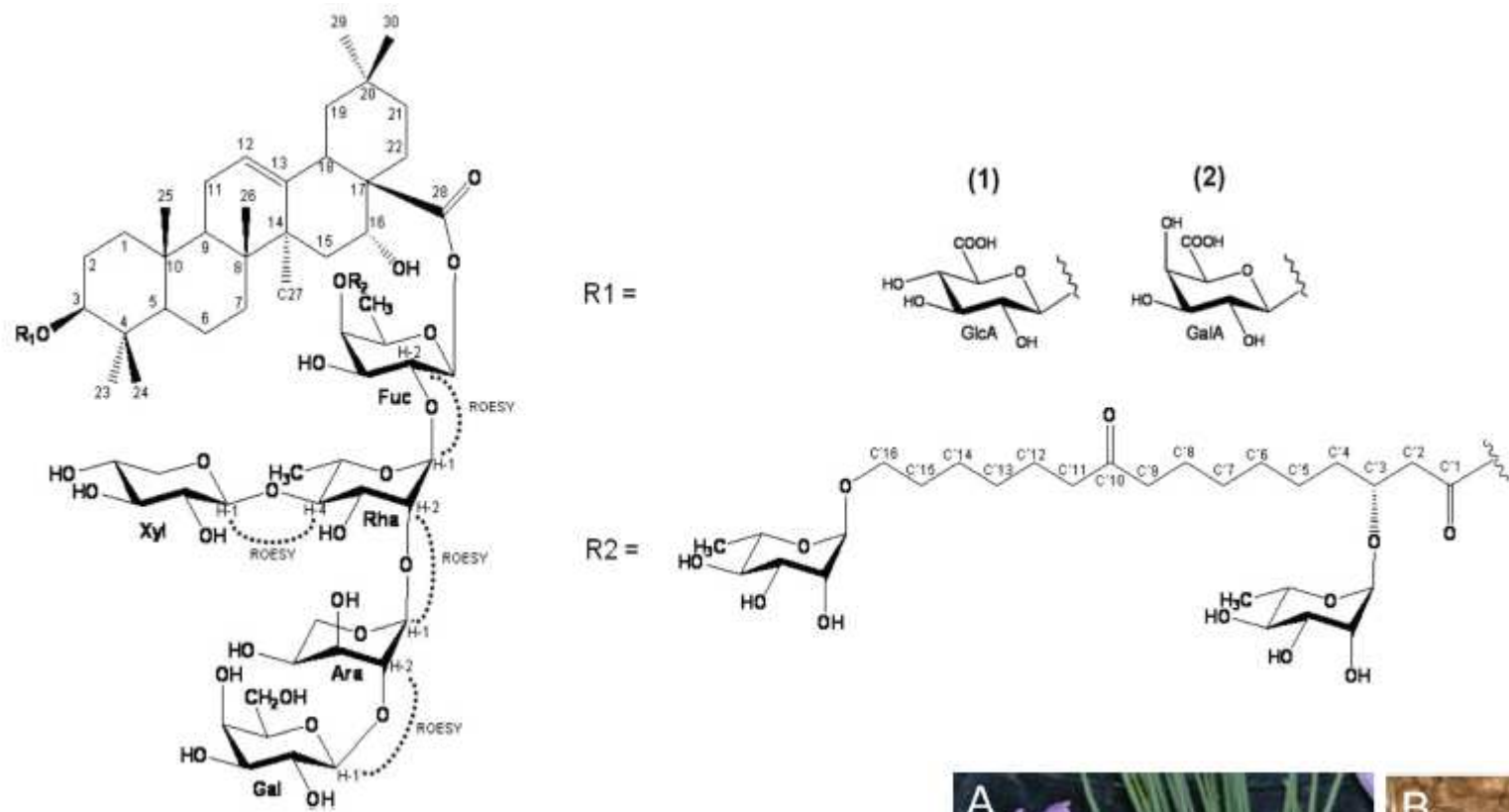


Figure 7. Structures of the triterpenic saponins, azafraines 1 and 2, identified in the corn.

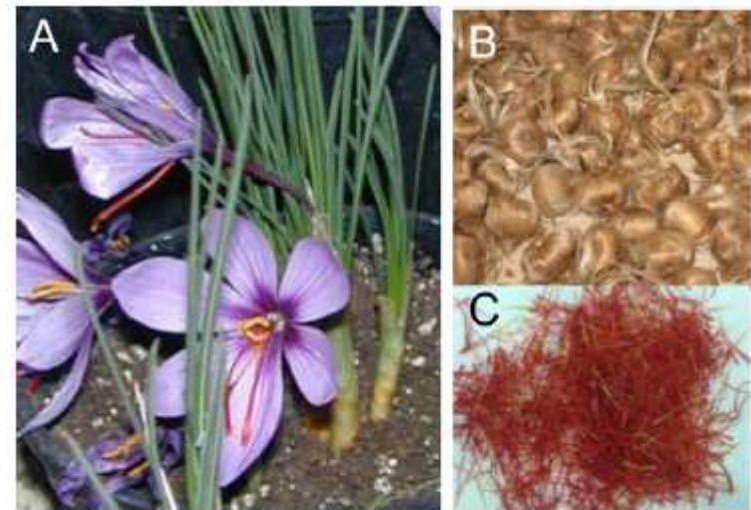


Figure 1. Most valuable parts of *Crocus sativus*: (A) saffron flowers; (B) combs; (C) stigma.

IMPRESSIONS OF SOME OF THE NEWER DRUGS IN DERMATOLOGICAL PRACTICE

Allen, Charles W. *Medical Record* (1866-1922); *New York* 42.4 (Jul 23, 1892): 92.

The odor is said to resemble **saffron**



IMPRESSIONS OF SOME OF THE NEWER DRUGS IN DERMATOLOGICAL PRACTICE.*

By CHARLES W. ALLEN, M.D.,

ASSISTANT TO THE CHIEF MEDICAL OFFICER, NEW-YORK HOSPITAL.

There is no doubt that many of the specialties of this age are but renovated antiquae, still the most firm believers in the adage that there is nothing new under the sun, will scarcely claim that the "new" remedies of the last few years—many of them purely the result of synthetic logic thought as well as of chemical manipulations—were ever made by mortal man before, or ever used to cure his ill. Never before in the whole history of medicine have remedies been multiplied with such profusion. Before we have had time to familiarize ourselves with the name of the preparation, much less with its supposed virtues, it has, in many instances, been heralded in an avalanche of similar remedies for the same purpose—but better—and not always, as one would suppose, introduced by a rival manufacturing firm. Much disappointment is often caused to those who, desiring to use the best, and conscious of the inadequacy of the old, turn to a new remedy which has been heralded by its discoverer, widely advertised by its manufacturer, and whose wonderful effects have been loudly proclaimed by subsidized or deluded journals.

The object of the present communication is to give my impressions of some of the newer remedies for external use, especially in skin diseases, which are not so new but that they have stood the test of time, and to indicate those which the writer has found to possess at least sufficient good qualities to secure for them a place in the list of valuable therapeutic agents.

Naphthol may still be classed among the newer remedies which have not gone to the wall, and while one of the most powerful and safest antiseptics of the phenol series it has not superseded carbolic acid in surgery, as it was at one time thought it might, and still remains a very valuable agent in the treatment of many forms of cutaneous disease.

Five years ago, I believe this very month, I had the privilege of addressing this Society on the subject of Naphthol in *Dermatology*, and since that time I have continued to employ it in many of the skin affections in which I had till then noted its good effects, and have extended its use to some other conditions. Thus in the parasitic diseases, notably scabies, its action is uniformly favorable, and is increased when combined with sulphur. In pruritic affections, and in pruritus without lesions, it often cures the itching when other remedies have failed. In institution practice I place reliance on an empyretic oil containing ten per cent. of naphthol. Occasional failures occur, as with any other incalculating remedy.

In diseases of the scalp, psoriasis, seborrhea, seborrhoeal eczema, impetiginous eczema, pediculosis, psoriasis, alopecia, and alopecia areata, I may say naphthol has given me as general satisfaction as any other single remedy. I now, more than formerly, combine the hydrochloride of mercury with it in several of these conditions, and with increased effect. If alopecia is due to any of these diseases, then naphthol tends to check the loss of hair by making the scalp healthy. The stimulating effect upon the healthy scalp has, it seems to me, prevented further loss of hair in many cases, and in some instances has undoubtedly brought about an increased growth. I believe, too, it hastens the natural return of the hair in syphilitic alopecia, as well as that following erysipelas, typhoid, and other debilitating forms of sickness. In women especially, hair renewed growth of hair has been at times very prompt and satisfactory in the ordinary forms of alopecia. In syphilitic alopecia I have had several recoveries after a course of treatment both surprising to me and gratifying to the patient, by reason of its inertness.

* First before the *Michigan Medical and Surgical Society*, May, 1884. *Medical Record*, May 24, 1884.

In such obstinate diseases as ichthyosis and prurigo of Hebra the results have been very satisfactory, while in milder affections, such as acne, chromophthoria, ringworm, psoriasis, etc., naphthol has its use.

A good prescription is:

R. Naphthol liq. ʒi ss.
 Ethyl. acet. ʒi (or ʒi ss.)
 Lanolin. ʒi
 Camellia. ʒi

M. For scabies the proportion of naphthol can be increased to ten per cent.

The following is the prescription which I have mostly used for the scalp:

R. Naphthol liq. ʒi to ʒi ss.
 Ol. Olive. ʒi ss.
 Ol. sweetgum. ʒi
 Ol. sweetgum. ʒi ss.
 Spt. vin. ros. ʒi ss.

M. To be applied to scalp once daily.

In the full strength, I have once seen an eczema produced in a scalp the rest of pityriasis.

A practical point in regard to the way ointments should be made. I often see ointments dispensed with the naphthol crystals simply suspended in the base, and this may account for many failures put down to the inefficacy of the drug. Now, while but slightly soluble in water, it is freely so in alcohol, ether, chloroform, benzole, etc., and it should be ordered to be first dissolved in one of these before mixing with the base, or the druggist will probably neglect it. Perhaps as good a plan as any is that suggested by Hardy, of dissolving in ether, then evaporating the ether with heat before adding the fatty base. I have made extensive use of naphthol soap (two and a half per cent.), with or without sulphur, in parasitic diseases, acne, dry scaly conditions, pityriasis rosea, and pruritus, with often decided benefit. Iodo-naphthol, betol, benzoate of naphthol, and camphorated naphthol, are recently introduced modifications which have not yet come much into use, but the last mentioned compound has already some reputation as an inert antiseptic in tuberculous abscesses.

Oxydide of Benzoin.—This is a drug which has come into use in certain quarters without the aid of literature. At least I have seen scarcely anything written upon the subject. I think it must be at least five years since my attention was directed to what was then rather a new preparation for wound treatment. It occurs as an insoluble powder of a bright coppery-red color, and is without odor. It can be prepared by fusing iodine with bisulphur, forming bisulphur iodide, and heating in water, when the subiodide precipitates. Another mode of preparation for small quantities which has been given is by the following formula:

R. Benzoin sublim. ʒi (or ʒi ss.)
 Aq. stibic. ʒi
 Aq. liq. ʒi
 M. Dissolve with heat in potassium iodide, add water slowly, and stir.
 R. Potash iod. ʒi (or ʒi ss.)
 Aq. liq. ʒi
 M. Add in part first, agitating after each addition, stir, and add precipitate with boiling water.

So favorable was my impression of this preparation from the first, for the treatment of ulcerative lesions, that I introduced it in three public institutions where up to that time it had not been known, and in spite of its expense it has continued to be much employed and has grown in favor. Although it may be used in the form of an ointment it about ten per cent. strength, my chief experience has been with it as a powder dressing; sprinkled lightly over an ulcer, excoriation, scalding wound, sloughing venereal sore, or any other raw surface, it forms a glaze-like covering of metallic lustre which is protective at the same time that it exerts an antiseptic, a some

UNITED STATES PATENT OFFICE

1,943,467
PHARMACEUTICAL PREPARATION
Rudolph S. Bley, Washington, D. C.
No Drawing. Application February 8, 1932
Serial No. 501,755
18 Claims (Cl. 167...)



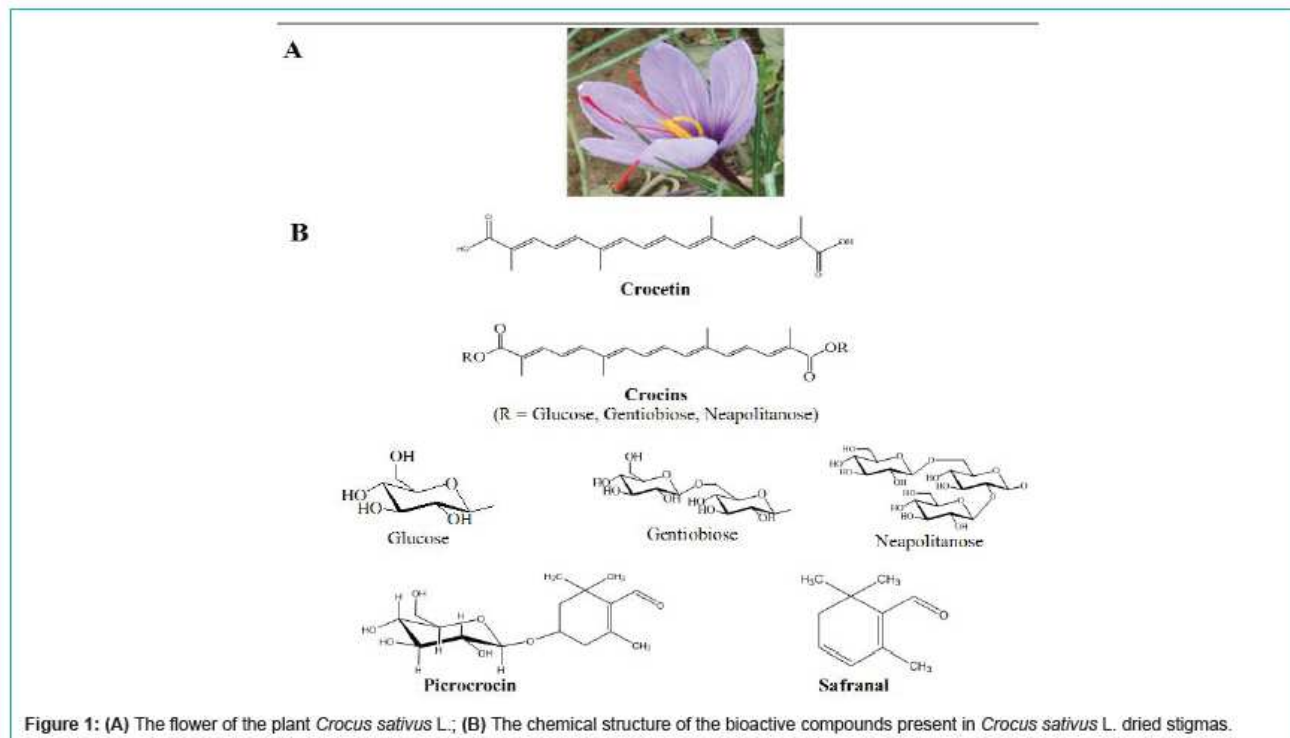
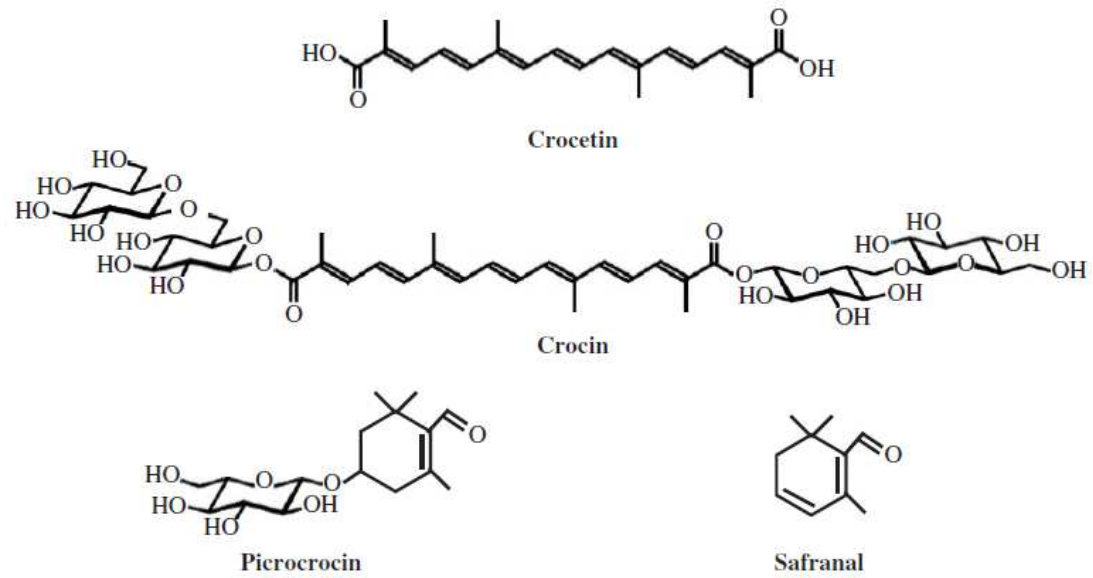
Other modifying and flavoring compounds may be incorporated, such as cream of tartar, sodium bicarbonate, borax, saccharine, sodium chloride, boric acid, milk sugar, glucose, higher sugars,

starches, saponins, quinine, quinine derivatives, glucosides, peppermint oil, peppermint oil substitutes, clove oil, eucalyptol, terpenyl acetate, cassia oil, cinnamon oil, thyme oil, nutmeg oil, anethol, camphor, eugenol, phenethyl alcohol, Caraway oil, orris root powder, alcohols, bergamot oil, rose-geranium oil, neroli oil, citronellol, benzaldehyde, albumina, myrrh powder, menthol, methyl salicylate, thymol, geraniol, lavender oil, lemon oil, citral, eosine, salol, phloxine, magenta crystals, erythrosine, sodium benzoate, carmine, saffron, glycerine, glycerine of starch, glycerine substitutes, honey, syrup, molasses, levulose, gums, vitamins, irradiated vitamins, radioactive substances, enzymes, ferments, buffer salts, etc. ...

Chemotherapy of Tuberculosis

HML Riggins, RP Gearhart - Medical Clinics of North America, 1947 - Elsevier

... A better understanding of the mechanism of action of antibacterial agents, although obviously not essential to the even greater success of chemotherapy, nevertheless ... and upon the top of all lay of Shavings of Hartshorn half a Pound, of Cloves an Ounce, of Saffron three Drams. ...



25

Amazing Benefits Of **SAFFRON** For Skin, Hair, And Health

- Disease Prevention
- Volatile Oils
- Active Components
- Therapeutic Applications
- Antidepressant
- Digestive Properties
- Cell Formation And Repair
- Heart Diseases And Blood Pressure
- Blood Cell Production
- Optimum Health
- Weight Loss And Diet Control
- Respiratory Health
- Mental Health
- Sexual Health
- Combating Diabetes



STYLECRAZE



SUPERFOOD SAFFRON

Improves Brain
Function and lifts your
spirit



Antioxidant Properties

Protects your Eyes

QUICK TIPS

Organic Category I
is the best grade
available

Make it go further
by crushing the
saffron in the palm
of your hand
before using

Add to rice,
seafood, desserts
& tea

Excellent when
paired with Coorg
Cardamom or True
Cinnamon

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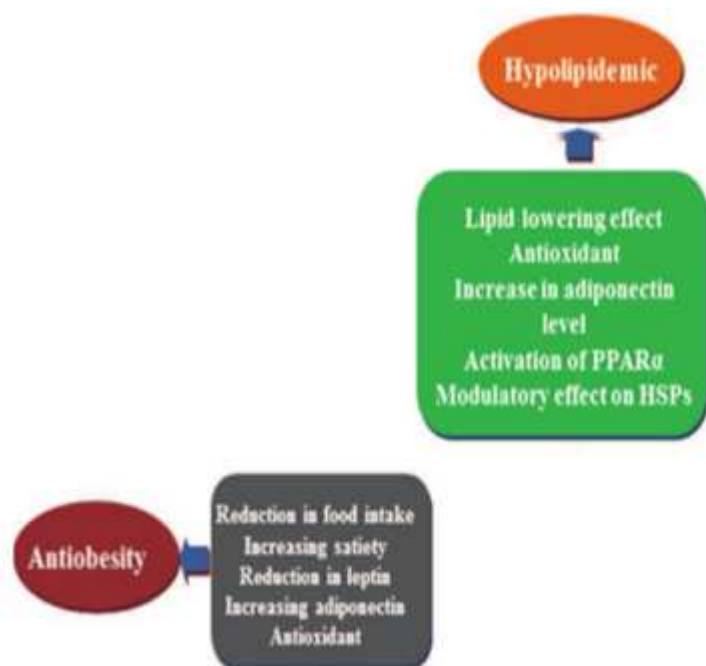


Obesidad

Review

Saffron: A Natural Potent Antioxidant as a Promising Anti-Obesity Drug

Maryam Mashmoul¹, Azrina Azlan^{1,2,*}, Huzwah Khaza'ai³, Barakatun Nisak Mohd Yusof¹ and Sabariah Mohd Noor⁴



Abstract: Obesity is associated with various diseases, particularly diabetes, hypertension, osteoarthritis and heart disease. Research on possibilities of herbal extracts and isolated compounds from natural products for treating obesity has an upward trend. Saffron (*Crocus Sativus* L. *Iridaceae*) is a source of plant polyphenols/carotenoids, used as important spice and food colorant in different parts of the world. It has also been used in traditional medicine for treatment of different types of illnesses since ancient times. Many of these medicinal properties of saffron can be attributed to a number of its compounds such as crocetin, crocins and other substances having strong antioxidant and radical scavenger properties against a variety of radical oxygen species and pro-inflammatory cytokines. The aim of this article is to assess the potential role of saffron and its constituents in the regulation of metabolic functions, which can beneficially alter obesity pathophysiology.



Obesidad

Hipertensión



Obesidad

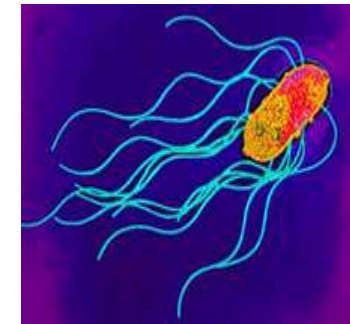
Hipertensión

Antibacteriano



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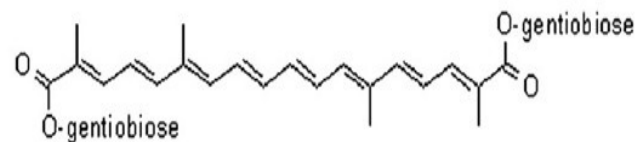
Food Control

journal homepage: www.elsevier.com/locate/foodcont

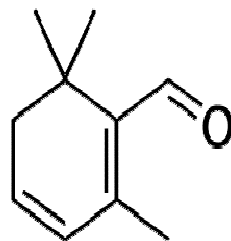
Short Communication

Bactericidal effect of saffron (*Crocus sativus* L.) on *Salmonella enterica* during storage

Concepción Pintado^a, Alicia de Miguel^a, Olga Acevedo^b, Leonor Nozal^b, José Luis Novella^b, Rafael Rotger^{a,*}



Crocin



Safranal

ABSTRACT

The presence of pathogenic bacteria in spices represents a public health risk as a possible cause of food contamination. *Salmonella* has been found in several spices and it has been involved in food-borne outbreaks, but this bacterium has not been reported as a contaminant of saffron (*Crocus sativus* L.). We examined a possible antibacterial effect of saffron using samples from Iran, Greece and Spain which were artificially contaminated with clinical isolates belonging to five different serovars of *Salmonella*. We detected a loss of viability during the room-temperature storage of the saffron samples, with bacteria being undetectable at day 16 except in the case of the DT104 strain of the Typhimurium serovar, in all of the samples, and of the Hadar serovar in the Iranian sample, both of which gave negative culture at day 32. The laboratory strain LT2 of the Typhimurium serovar was undetectable at day 4. To gain an insight into the basis for this bactericidal effect, we measured the inhibitory and bactericidal concentrations of safranal and crocin, the main compounds responsible for the flavouring and colouring capabilities of saffron. They were in the order of 8–16 mg/ml and 64–128 mg/ml for safranal and crocin, respectively. These data suggest that these compounds, and probably their chemical relatives, are involved in the antibacterial activity of saffron, and that this effect can significantly reduce the risk of food contamination with *Salmonella* by this spice.

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Asian Pacific Journal of Tropical Biomedicine

journal homepage: www.elsevier.com/locate/apjtbOriginal article <http://dx.doi.org/10.1016/j.apjtb.2016.12.014>

Green synthesis of silver nanoparticles using aqueous extract of saffron (*Crocus sativus* L.) wastages and its antibacterial activity against six bacteria



Ghodsieh Bagherzade^{1*}, Maryam Manzari Tavakoli¹, Mohmmad Hasan Namaci²

¹Department of Chemistry, College of Science, University of Birjand, Birjand 97179-414, Iran

²Hepatitis Research Center, Birjand University of Medical Sciences, Birjand 97179-414, Iran

ABSTRACT

Objective: To synthesis silver nanoparticles (AgNPs) by using extract of saffron (*Crocus sativus* L.) wastages and to test their antibacterial activity against six bacteria.

Methods: In this paper, the synthesis of AgNPs using aqueous extract of saffron wastage as a green method without any chemical stabilizer and reducer is demonstrated. The synthesized AgNPs were determined by UV-vis spectrum, high resolution transmission electron microscopy, X-ray diffraction, and Fourier transmission infrared spectroscopy analysis.

Results: UV-vis spectrum showed a peak at 450 nm due to excitation of surface plasmon vibrations. Fourier transmission infrared spectroscopy showed that nanoparticles were capped with plant secondary metabolites. X-ray diffraction analysis also demonstrated that the size range of the synthesized nanoparticles was 12–20 nm. Transmission electron microscope image illustrated AgNPs with spherical shape and an average size of 15 nm. The result of antibacterial activities showed that the biosynthesized AgNPs had an inhibiting activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Shigella flexneri* and *Bacillus subtilis*.

Conclusions: The biosynthesized AgNPs showed significant antibacterial effect against *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Shigella flexneri* and *Bacillus subtilis*, so, it can be used in biomedical applications.

Escherichia coli
Pseudomonas aeruginosa
Klebsiella pneumonia
Shigella flexneri
Bacillus subtilis



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Journal of Cleaner Production

journal homepage: www.elsevier.com/locate/jclepro



Assessment of antibacterial activity of wool fabrics dyed with natural dyes



Fatemeh Shahmoradi Ghaheh^a, Sayed Majid Mortazavi^{a,*}, Farzaneh Alihosseini^a, Afshin Fassihi^b, Ali Shams Nateri^c, Daryoush Abedi^d



Highlights

- Antibacterial activity of wool dyed with natural dyes was tested against *some bacteria*.
- The antibacterial activity and durability of them is enhanced using alum mordant.
- 100% antibacterial activity even after 5 washes or exposure to light for 300 min.
- The cost of natural dyeing was approximately the same as the cost of acid dyeing.

Staphylococcus aureus
Pseudomonas aeruginosa
Escherichia coli

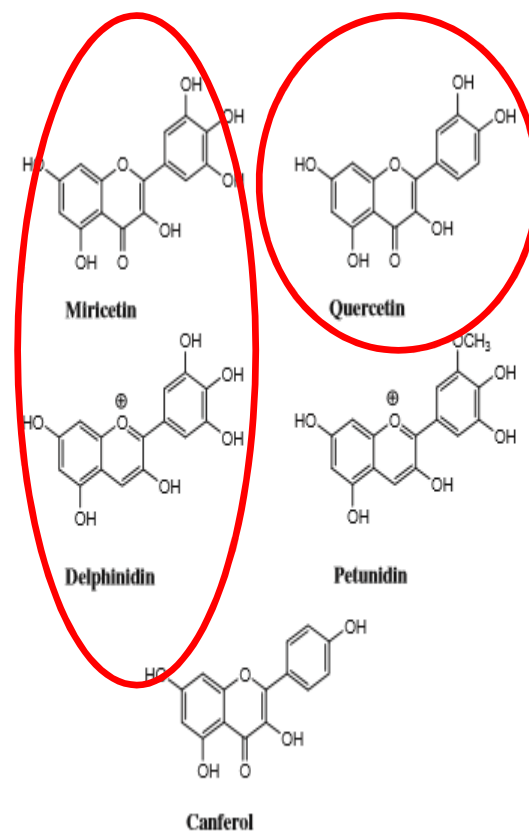
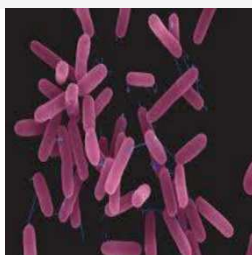


Fig. 6. Chemical structure of the main components of saffron petals (Kubo and Kinst-Hori, 1999).



Safranal and its analogs inhibit *Escherichia coli* ATP synthase and cell growth



Mason Liu, Amon Amini, Zulfiqar Ahmad*

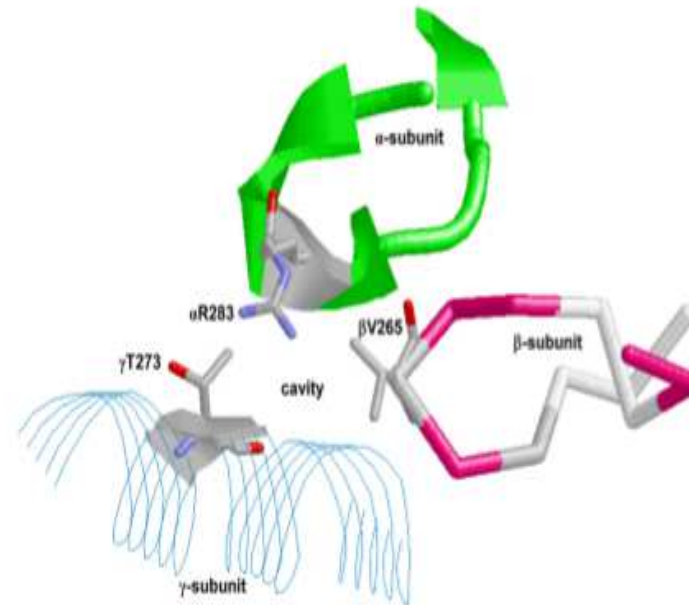


Fig. 3. X-ray crystallographic structure of the polyphenol binding pocket of F_1F_0 ATP synthase. α -, β -, and γ -subunits forming an inhibitor binding cavity are shown. Some residues, including α Arg-283, are identified. The figure was generated by PDB file 2J11 [11] using RasMol software. Residue numbers are based on *E. coli* numbering.



Obesidad

Hipertensión

Antibacteriano

Ulceras

Inhibition of *Helicobacter pylori* Growth *in vitro* by Saffron (*Crocus sativus* L.)

¹Mahboobeh Nakhaei, ²Mehrangiz Khaje-Karamoddin, ^{*3}Mohammad Ramezani

Abstract

Objective(s)

Anti-*Helicobacter pylori* effects of saffron (*Crocus sativus* L., Iridaceae) and its major constituents, crocin and safranal, were evaluated.

Materials and Methods

Macerated aqueous and methanol extracts tested against 45 clinical isolates of *Helicobacter pylori*, using paper disc diffusion method (DDM) on modified egg yolk emulsion agar (EYE agar). Four antibiotics also tested against all isolates as positive control.

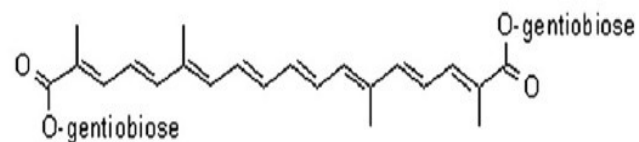
Results

Although there were small differences in sensitivity among the isolates tested, but all isolates were susceptible to methanol and aqueous extracts. The minimum inhibitory concentrations (MIC) of methanol extract, crocin and safranal measured as 677, 26.5 and 16.6 $\mu\text{g/ml}$, respectively, using agar dilution method. The results showed that high temperature did not have any effect on the activity of extracts, crocin and safranal. The effect of pH on the activity of methanol extract indicated no significant difference at pH 5 to 8, in comparison with the control.

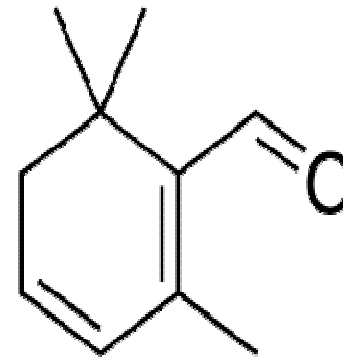
Conclusion

The results indicated that saffron has a moderate anti-*Helicobacter* activity.

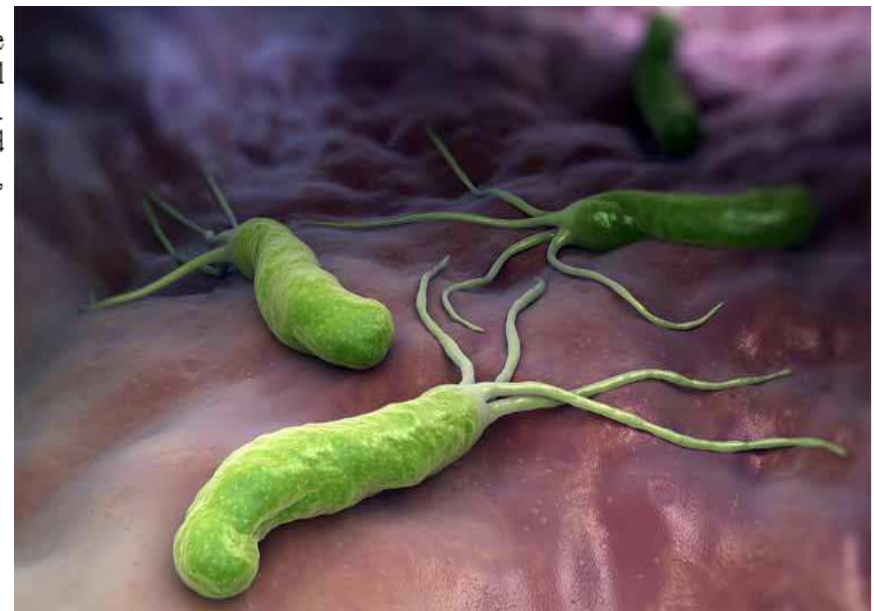
Keywords: Anti-*Helicobacter pylori*, Crocin, *Crocus sativus*, Saffron, Safranal



Crocin



Safranal





Obesidad

Hipertensión

Antibacteriano

Ulceras

Antioxidante



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Materials Science and Engineering C

journal homepage: www.elsevier.com/locate/msec

Nanostructured lipid dispersions for topical administration of crocin, a potent antioxidant from saffron (*Crocus sativus* L.)



Elisabetta Esposito ^{a,*}, Markus Drechsler ^b, Paolo Mariani ^c, Anna Maria Panico ^d, Venera Cardile ^e, Lucia Crascì ^d, Federica Carducci ^c, Adriana Carol Eleonora Graziano ^e, Rita Cortesi ^{a,*}, Carmelo Puglia ^d

Crocin, a potent antioxidant obtained from saffron, shows anticancer activity in *in vivo* models. Unfortunately unfavorable physicochemical features compromise its use in topical therapy.

The present study describes the preparation and characterization of nanostructured lipid dispersions as drug delivery systems for topical administration of crocin and the evaluation of antioxidant and antiproliferative effects of crocin once encapsulated into nanostructured lipid dispersions.

Nanostructured lipid dispersions based on monoolein in mixture with sodium cholate and sodium caseinate have been characterized by cryo-TEM and PCS. Crocin permeation was evaluated *in vitro* by Franz cells, while the oxygen radical absorbance capacity assay was used to evaluate the antioxidant activity. Furthermore, the antiproliferative activity was tested *in vitro* by the MTT test using a human melanoma cell line.

The emulsification of monoolein with sodium cholate and sodium caseinate led to dispersions of cubosomes, hexosomes, sponge systems and vesicles, depending on the employed emulsifiers. Permeation and shelf life studies demonstrated that nanostructured lipid dispersions enabled to control both rate of crocin diffusion through the skin and crocin degradation. The oxygen radical absorbance capacity assay pointed out an interesting and prolonged antioxidant activity of crocin while the MTT test showed an increase of crocin cytotoxic effect after incorporation in nanostructured lipid dispersions.

This work has highlighted that nanostructured lipid dispersions can protect the labile molecule crocin from degradation, control its skin diffusion and prolong antioxidant activity, therefore suggesting the suitability of nanostructured lipid dispersions for crocin topical administration.



Obesidad

Hipertensión

Antibacteriano

Ulceras

Antioxidante

Diabetes



Saffron (*Crocus sativus* L.) increases glucose uptake and insulin sensitivity in muscle cells via multipathway mechanisms

Changkeun Kang^a, Hyunkyung Lee^a, Eun-Sun Jung^a, Ramin Seyedian^{a,1}, MiNa Jo^a, Jehin Kim^a, Jong-Shu Kim^a, Euikyung Kim^{a,b,*}

^aCollege of Veterinary Medicine, Gyeongsang National University, Jinju 660-701, South Korea

^bResearch Institute of Life Science, Gyeongsang National University, South Korea

ABSTRACT

Saffron (*Crocus sativus* Linn.) has been an important subject of research in the past two decades because of its various biological properties, including anti-cancer, anti-inflammatory, and anti-atherosclerotic activities. On the other hand, the molecular bases of its actions have been scarcely understood. Here, we elucidated the mechanism of the hypoglycemic actions of saffron through investigating its signaling pathways associated with glucose metabolism in C₂C₁₂ skeletal muscle cells. Saffron strongly enhanced glucose uptake and the phosphorylation of AMPK (AMP-activated protein kinase)/ACC (acetyl-CoA carboxylase) and MAPKs (mitogen-activated protein kinases), but not PI 3-kinase (Phosphatidylinositol 3-kinase)/Akt. Interestingly, the co-treatment of saffron and insulin further improved the insulin sensitivity via both insulin-independent (AMPK/ACC and MAPKs) and insulin-dependent (PI 3-kinase/Akt and mTOR) pathways. It also suggested that there is a crosstalk between the two signaling pathways of glucose metabolism in skeletal muscle cells. These results could be confirmed from the findings of GLUT4 translocation. Taken together, AMPK plays a major role in the effects of saffron on glucose uptake and insulin sensitivity in skeletal muscle cells. Our study provides important insights for the possible mechanism of action of saffron and its potential as a therapeutic agent in diabetic patients.

Effects of Cinnamon, Cardamom, Saffron, and Ginger Consumption on Markers of Glycemic Control, Lipid Profile, Oxidative Stress, and Inflammation in Type 2 Diabetes Patients

Paria Azimi^{1,2}, Reza Ghiasvand^{1,2}, Awat Feizi^{1,2}, Mitra Hariri^{1,2}, Behnoud Abbasi^{1,2}

¹Food Security Research Center, Isfahan University of Medical Science, Isfahan, Iran. ²Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Science, Isfahan, Iran. Address correspondence to: Reza Ghiasvand, e-mail: ghiasvand@hih.mui.ac.ir

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■ Abstract

OBJECTIVES: Type 2 diabetes (T2D) may be caused by elevated oxidative stress, inflammation, and hyperglycemia. The phytochemicals in several herbal medicines are reported to effectively improve diabetes and to ameliorate diabetic complications. The aim of the present study was to determine the effects of cinnamon, cardamom, saffron, and ginger as supplementary remedies in T2D. **METHODS:** This randomized controlled, clinical trial included 204 T2D patients. The participants were randomly assigned to four intervention groups receiving 3 glasses of black tea and either 3 g cardamom, or cinnamon, or ginger, or 1 g saffron and one control group which consumed only 3 tea glasses without any herbal medicine for 8 weeks. Markers of inflammation, oxidative stress, fasting blood sugar, lipid profile, and anthropometric measures were evaluated at base-

line and after 8 weeks of intervention. **RESULTS:** After 8 weeks of intervention, cinnamon, cardamom, ginger, and saffron consumption had significant effects on total cholesterol, LDL, and HDL levels ($p < 0.05$) compared with controls. However, the herbal products did not have significant effects on measures of glycemic control, anthropometry, inflammation, and oxidative stress. In within-group comparisons only, cinnamon intake significantly decreased fasting blood sugar (FBS). **CONCLUSIONS:** The herbal remedies examined had significantly beneficial effects on cholesterol, but not on measures of glycemic control, oxidative stress, and inflammation. Based on the contradictory results reported in the literature, the effects of herbal medicine in diabetic patients should undergo further detailed investigation.

Keywords: type 2 diabetes · herbal medicine · cholesterol · glycemic control · oxidative stress · inflammation



Beneficial impact of crocetin, a carotenoid from saffron, on insulin sensitivity in fructose-fed rats

Liang Xi^a, Zhiyu Qian^{a,*}, Guanglin Xu^b, Shuguo Zheng^a, Sai Sun^a, Na Wen^a, Liang Sheng^a, Yun Shi^a, Yabing Zhang^a

^aDepartment of Pharmacology, China Pharmaceutical University, Nanjing 210009, PR China

^bCollege of Life Science, Nanjing Normal University, Nanjing 210097, PR China

Received 29 December 2005; received in revised form 6 March 2006; accepted 23 March 2006

Abstract

Crocetin, a unique carotenoid with potent antioxidative and anti-inflammatory activities, is a major ingredient of saffron which is used as an important spice and food colorant in various parts of the world. In the present study, the effect of crocetin on insulin resistance and its related abnormalities induced by high-fructose diet were investigated in male Wistar rats. Compared to the control rats fed on normal laboratory diet, fructose-fed rats developed a series of pathological changes including insulin resistance, hyperinsulinemia, dyslipidemia and hypertension. Although having no evident effect on the body weight, fructose feeding caused a marked increase in the weight of epididymal white adipose tissue. Furthermore, a significant reduction in the expression of both protein and mRNA of adiponectin (an insulin-sensitizing adipocytokine) was observed, whereas those of tumor necrosis factor (TNF)- α and leptin were enhanced in epididymal white adipose tissue in fructose-fed rats. These disorders were effectively normalized in crocetin-treated rats. Crocetin was also demonstrated here to alleviate free fatty acid (FFA)-induced insulin insensitivity and dysregulated mRNA expression of adiponectin, TNF- α and leptin in primary cultured rat adipocytes. These findings suggest the possibility of crocetin treatment as a preventive strategy of insulin resistance and related diseases. The favorable impact on adiponectin, TNF- α and leptin expression in white adipose tissue may be involved in the improvement of insulin sensitivity observed in crocetin-treated rats.

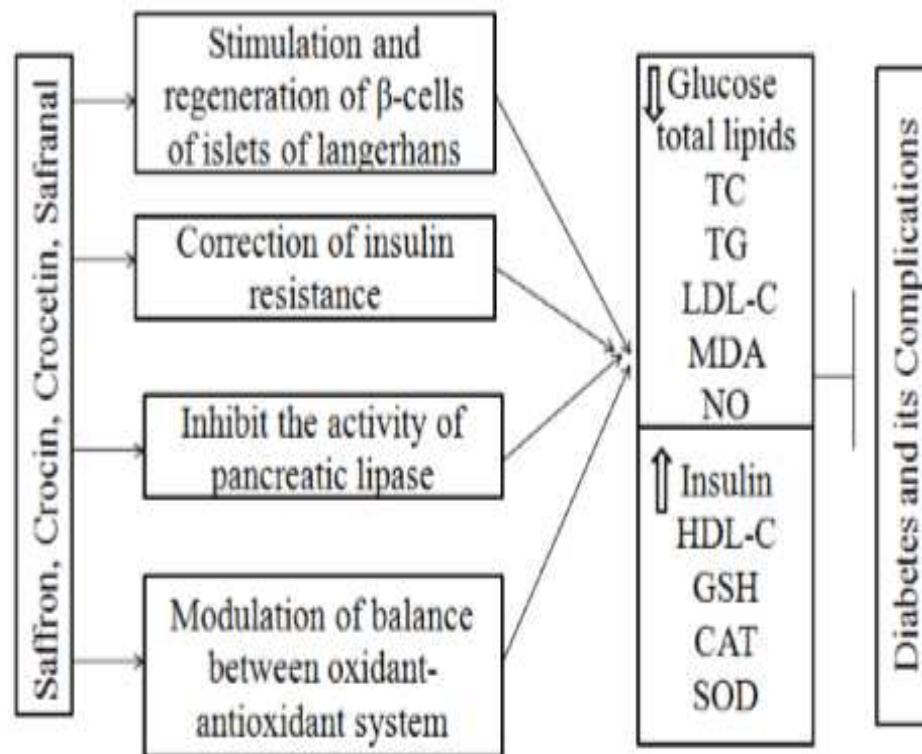
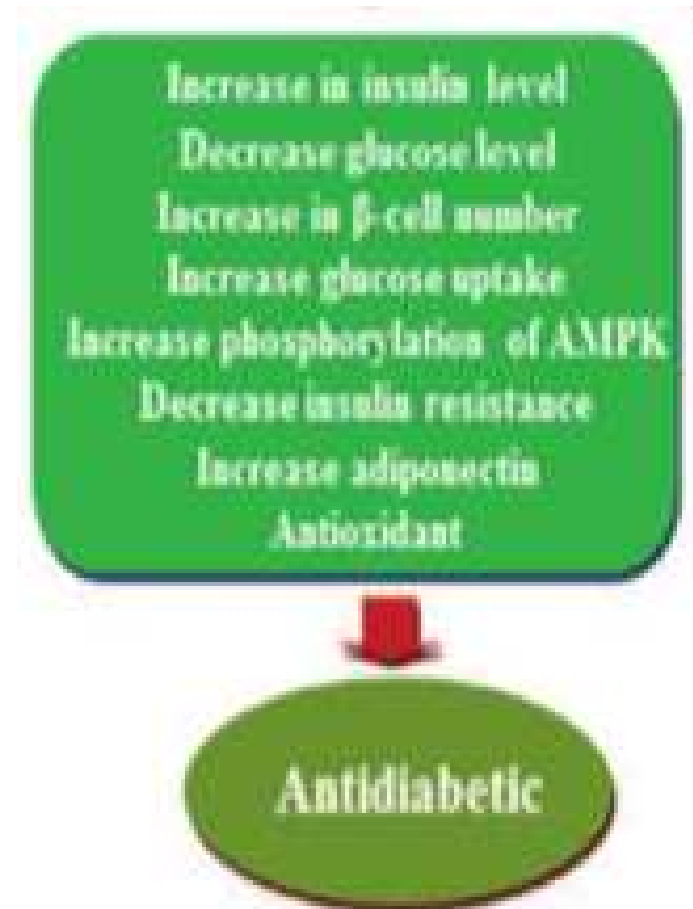


Figure 2. The molecular targets of diabetes and its complications modulated by saffron and its main ingredients.



Saffron (*Crocus sativus* L.) Powder as an Ingredient of Rye Bread: An Anti-Diabetic Evaluation

To cite this article:

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Lussekatte o pan de azafrán

In this study, a most consumer-acceptable rye bread (RB) containing saffron (S) powder (RB+S) was designed to verify its anti-diabetic properties, and to compare these effects with those of RB and S separately, matched to a similar dose of bioactive components, used in the high-fat (HF) diet in streptozotocin (STZ)-induced Wistar rats. After baking, beneficial antioxidant and sensory properties for RB enriched with 0.12% S were achieved. Twenty-four severely diabetic rats (fasting blood glucose (FBG) ≥ 350 mg/dL) were randomized to incorporate either 0.08% of pure S, or RB enriched with 0.12% S (the diet provided 0.08% of S), or RB alone into their diet for 5 weeks. As controls, nontreated, HF-feeding STZ-induced rats (positive control-HF/STZ) and rats receiving normal laboratory diet (negative control-C) were used. A significant FBG-lowering effect was observed (47%, 53%, and 54% reduction vs. HF/STZ; $P < .05$) after S, RB, and RB+S treatment. Improvements in the rats' glycemia were achieved by β -cell regeneration and increases in insulin secretion. Only in the S and RB+S group of rats, a significant ($P < .05$) increase in relative pancreas (vs. HF/STZ) was noted. A significant ($P < .05$) reduction in the concentration of thiobarbituric acid-reactive substances (TBARS) was achieved, whereas the ferric-reducing ability of plasma (FRAP) was not changed after S, RB and RB+S treatment (vs. HF/STZ). Triglyceride (TG) concentrations after S, RB, and RB+S treatment were significantly decreased ($P < .05$) versus HF/STZ. Both S and RB can be used in diabetic therapy, but no additional metabolic effect was achieved after consumption of RB+S.



Obesidad

Hipertensión

Antibacteriano

Ulceras

Antioxidante

Diabetes

Anticancerígeno



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Cancer Letters 100 (1996) 23–30

**CANCER
LETTERS**

Crocin, safranal and picrocrocin from saffron (*Crocus sativus* L.) inhibit the growth of human cancer cells in vitro

Julio Escribano^a, Gonzalo-Luis Alonso^b, Miguel Coca-Prados^c,
José-Antonio Fernández^{a,*}

Abstract

Extracts of saffron (*Crocus sativus* L.) have been reported to inhibit cell growth of human tumor cells. In order to study the cytotoxic effect of the characteristic compounds of saffron spice, we have isolated crocin, crocetin, picrocrocin and safranal. Doses inducing 50% cell growth inhibition (LD₅₀) on HeLa cells were 2.3 mg/ml for an ethanolic extract of saffron dry stigmas, 3 mM for crocin, 0.8 mM for safranal and 3 mM for picrocrocin. Crocetin did not show cytotoxic effect. Cells treated with crocin exhibited wide cytoplasmic vacuole-like areas, reduced cytoplasm, cell shrinkage and pyknotic nuclei, suggesting apoptosis induction. Considering its water-solubility and high inhibitory growth effect, crocin is the more promising saffron compound to be assayed as a cancer therapeutic agent.

To our knowledge, this is the first report showing that saffron-induced antitumor effects may affect EMT processes. Specifically, we observed that the induction of epithelial differentiation was a time-dependent event and was evident from 4 days of treatment with SE and CR. Based on the current data, saffron and its ingredients could be considered as a promising candidate for clinical anticancer trials in aggressive prostate cancer with a high risk of metastases.



Research Article

Antitumor Effects of Saffron-Derived Carotenoids in Prostate Cancer Cell Models

Claudio Festuccia,¹ Andrea Mancini,¹ Giovanni Luca Gravina,^{1,2} Luca Scarsella,¹ Silvia Llorens,³ Gonzalo L. Alonso,⁴ Carla Tatone,⁵ Ernesto Di Cesare,⁶ Emmanuele A. Jannini,⁷ Andrea Lenzi,² Anna M. D'Alessandro,⁶ and Manuel Carmona^{4,8}

Crocus sativus L. extracts (saffron) are rich in carotenoids. Preclinical studies have shown that dietary intake of carotenoids has antitumor effects suggesting their potential preventive and/or therapeutic roles. We have recently reported that saffron (SE) and crocin (CR) exhibit anticancer activity by promoting cell cycle arrest in prostate cancer (PCa) cells. It has also been demonstrated that crocetin esters are produced after SE gastrointestinal digestion by CR hydrolysis. The aim of the present report was to investigate if SE, crocetin (CCT), and CR affected *in vivo* tumor growth of two aggressive PCa cell lines (PC3 and 22rv1) which were xenografted in male nude mice treated by oral gavage with SE, CR, and CCT. We demonstrated that the antitumor effects of CCT were higher when compared to CR and SE and treatments reverted the epithelial-mesenchymal transdifferentiation (EMT) as attested by the significant reduction of N-cadherin and beta-catenin expression and the increased expression of E-cadherin. Additionally, SE, CR, and CCT inhibited PCa cell invasion and migration through the downmodulation of metalloproteinase and urokinase expression/activity suggesting that these agents may affect metastatic processes. Our findings suggest that CR and CCT may be dietary phytochemicals with potential antitumor effects in biologically aggressive PCa cells.

Cancer Chemopreventive and Tumoricidal Properties of Saffron (*Crocus sativus* L.)

[Fikart I. Abdullaev](#)

Since cancer is the most common cause of death in the world population, the possibility that readily available natural substances from plants, vegetables, herbs, and spices may be beneficial in the prevention of cancer warrants closer examination. Saffron in filaments is the dried, dark red stigmas of *Crocus sativus* L. flowers and it is used as a spice, food colorant, and a drug in medicine. A growing body of research has demonstrated that saffron extract itself and its main constituents, the carotenoids, possess chemopreventive properties against cancer. This review discusses recent literature data and our results on the cancer chemopreventive activities of saffron and its main ingredients



Alzheimer

Obesidad

Hipertensión

Antibacteriano

Ulceras

Antioxidante

Diabetes

Anticancerígeno

A Perspective on *Crocus sativus* L. (Saffron) Constituent Crocin: A Potent Water-Soluble Antioxidant and Potential Therapy for Alzheimer's Disease

John W. Finley^{*,†,‡}  and Song Gao[§]

DOI: 10.1021/acs.jafc.6b04398
J. Agric. Food Chem. 2017, 65, 1005–1020

ABSTRACT: Alzheimer's disease (AD) is the most common form of dementia, in which the death of brain cells causes memory loss and cognitive decline. Several factors are thought to play roles in the development and course of AD. Existing medical therapies only modestly alleviate and delay cognitive symptoms. Current research has been focused on developing antibodies to remove the aggregates of amyloid- β ($A\beta$) and *tau* protein. This approach has achieved removal of $A\beta$; however, no cognitive improvement in AD patients has been reported. The biological properties of saffron, the dry stigma of the plant *Crocus sativus* L., and particularly its main constituent crocin, have been studied extensively for many conditions including dementia and traumatic brain injury. Crocin is a unique antioxidant because it is a water-soluble carotenoid. Crocin has shown potential to improve learning and memory as well as protect brain cells. A search of the studies on saffron and crocin that have been published in recent years for their impact on AD as well as crocin's effects on $A\beta$ and *tau* protein has been conducted. This review demonstrates that crocin exhibits multifunctional protective activities in the brain and could be a promising agent applied as a supplement or drug for prevention or treatment of AD.



Alzheimer

Afrodisíaco

Obesidad

Hipertensión

Antibacteriano

Ulceras

Antioxidante

Diabetes

Anticancerígeno



Phytomedicine

Volume 15, Issues 6–7, 20 June 2008, Pages 491–495

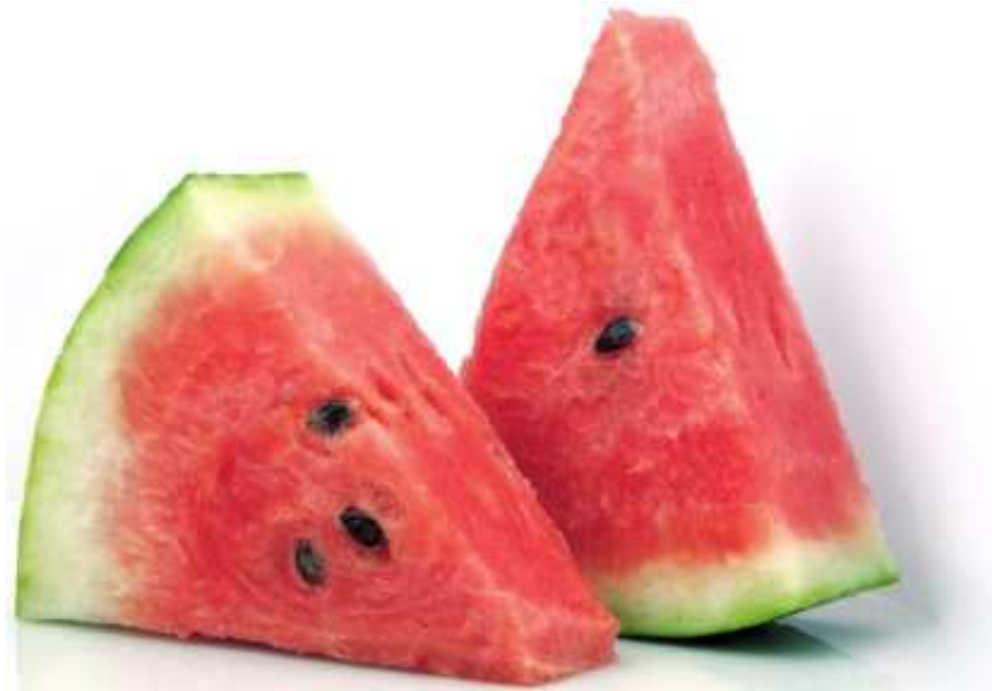


The effect of saffron, *Crocus sativus* stigma, extract and its constituents, safranal and crocin on sexual behaviors in normal male rats

H. Hosseinzadeh ^a  , T. Ziaee ^b, A. Sadeghi ^b

3 Junio 2008

La sandía, viagra natural



Es el mismo efecto que el ajo



**Evaluation of *Crocus sativus* L. (saffron) on male erectile dysfunction:
A pilot study**

Ali Shamsa^a, Hossein Hosseinzadeh^{b,*}, Mahmood Molaei^a,
Mohammad Taghi Shakeri^c, Omid Rajabi^d

Abstract

In this study, the effect of *Crocus sativus* (saffron) was studied on male erectile dysfunction (ED). Twenty male patients with ED were followed for ten days in which each morning they took a tablet containing 200 mg of saffron. Patients underwent the nocturnal penile tumescence (NPT) test and the international index of erectile function questionnaire (IIEF-15) at the start of the treatment and at the end of the ten days. After the ten days of taking saffron there was a statistically significant improvement in tip rigidity and tip tumescence as well as base rigidity and base tumescence. IIEF-15 total scores were significantly higher in patients after saffron treatment (before treatment 22.15 ± 1.44 ; after treatment 39.20 ± 1.90 , $p < 0.001$). Saffron showed a positive effect on sexual function with increased number and duration of erectile events seen in patients with ED even only after taking it for ten days.

A systematic review and meta-analysis of clinical trials on saffron (*Crocus sativus*) effectiveness and safety on erectile dysfunction and semen parameters

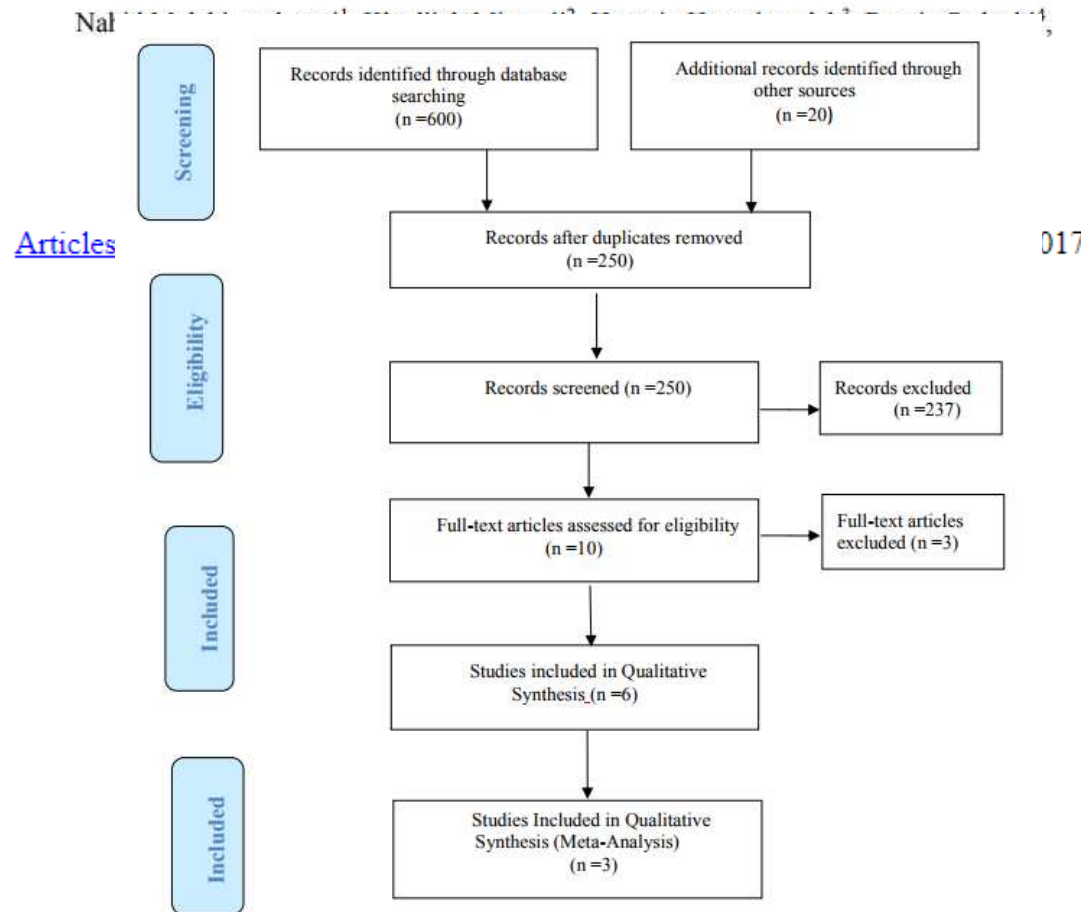


Figure 1. PRISMA Flowchart of the study selection process.

Abstract

Objective: We performed this systematic review and meta-analysis study to determine saffron (*Crocus sativus*) effectiveness and safety in male infertility problems.

Materials and Methods: The databases PubMed, Scopus, Cochrane, Google Scholar, SID, IranMedex and Magiran until July 2016 and reference section of relevant articles, were searched to find both English and Persian clinical trials on male infertility issues that used saffron as medical treatment. Also, the quality of these trials was evaluated by Oxford Center for Evidence Based Medicine checklist. A total of six trials was ultimately included. All statistical analyses were done by Comprehensive Meta-analysis (CMA) Version 2.

Results: Only in one study conducted on sperm parameters, the mean percentage of sperm with normal morphology ($p < 0.001$) and sperm motility ($p < 0.001$) were increased. Quantitative analysis showed that saffron had a significantly positive effect on all dimensions of Erectile Function questionnaire (MD for Erectile function=5.36($p=0.00$), Orgasmic function=1.12 ($p=0.007$), Overall satisfaction=1.23 ($p=0.005$), Satisfaction with intercourse=2.18 ($p=0.00$) and Sexual desire=0.78 ($p=0.00$), Fixed effects model using 3 trials). The result of subgroup analysis based on dimensions of Erectile Function questionnaire showed statistically significant differences among subgroups ($p=0.00$).

Conclusion: saffron has a positive effect on erectile dysfunction. However, our study showed contradictory results about semen parameters. So, interpretation of results is limited because of methodological flaws of the included studies, erectile dysfunction status and a large heterogeneity among them. Further trials are still needed to confirm the current findings.



Pre-supplementation of *Crocus sativus* Linn (saffron) attenuates inflammatory and lipid peroxidation markers induced by intensive exercise in sedentary women

Mohammad Hosseinzadeh¹, Hossein TaheriChadorneshin^{2*}, Mahboobe Ajam-Zibad³, Seyed-Hosein Abtahi-Eivary⁴

ABSTRACT

Antioxidant and anti-inflammatory actions of *Crocus sativus* Linn (saffron) in relation to intensive exercise need to be studied. This study aimed to investigate the effect of four weeks of saffron supplementation on serum levels of tumor necrosis factor alpha (TNF- α), as a marker of inflammation, malondialdehyde (MDA), as a marker of lipid peroxidation, and levels of Lactate dehydrogenase (LDH) and creatine kinase (CK), as two markers of muscle damage, in sedentary women following intensive exercise. After a 4-week period of supplementation (30 mg/day), the healthy inactive young women performed one bout of acute resistance exercises at 85 % of one-repetition maximum. Using commercial kits, TNF- α and MDA levels were measured using ELISA method. In addition, LDH and CK were measured by photometric method. Data were statistically analyzed by one-way ANOVA ($P < 0.05$). Our finding showed a significant increases in serum LDH ($P = 0.015$), CK ($P = 0.001$), TNF- α ($P = 0.001$) and MDA ($P = 0.001$) levels following one bout of resistance exercise. However, saffron supplementation prevent from increases in LDH ($P = 0.999$), CK ($P = 0.935$), TNF- α ($P = 0.898$) and MDA ($P = 0.617$) levels induced by one bout of resistance exercise. Although, intensive resistance exercise increases muscle damage enzymes, inflammatory and lipid peroxidation markers, however, pre-supplementation of saffron returns these markers to baseline levels. Therefore, it can be concluded that saffron supplementation acts as anti-oxidative and anti-inflammation agent, making it advisable to athletes and coaches involved in intensive resistance exercises.



THE APPLICATION OF CROCIN AND SAFFRON ETHANOL-EXTRACTABLE COMPONENTS IN FORMULATION OF HEALTH CARE AND BEAUTY CARE PRODUCTS

Author: H. Fekrat

Keywords: antioxidants, carotenoids, cosmetics, natural colors, skin cares, sun protection

DOI: [10.17660/ActaHortic.2004.650.46](https://doi.org/10.17660/ActaHortic.2004.650.46)

Abstract:

The characteristic yellow-orange color of saffron (*Crocus sativus* L.) comes from water-soluble pigment, the carotenoid crocin. Saffron carotenoids with ethanol-extractable mostly contain safranal as an antibacterial was used in Persian traditional medicine to treat some skin disorders. The extracted carotenoids from saffron as an antioxidant prevent many common diseases by taming harmful molecules known as free radicals. This paper reviews the application of saffron extracts from dried saffron stigmas by aqueous ethanol in formulation of cosmetics, skin cares and sun protection products.





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El **masaje** en la frente, o la aplicación de alguna pasta como la de sándalo, o la aplicación de *malai* o nata, calman el sistema y generan sensaciones agradables en el cerebro, lo que nos hace sentirnos bien. La aplicación de arcilla refresca. La aplicación de pasta de sándalo en la frente antes de la meditación es una práctica corriente en la India. Ayuda a meditar y a relajarse. *La pasta de sándalo se prepara frotando sobre una piedra un trozo de madera de sándalo al que se añaden unas gotas de agua, una pizca de alcanfor natural y una pizca de azafrán. Frotar hasta disolver el alcanfor y el azafrán. Añadir el agua necesaria.*









A Review on Medicinal Properties of Saffron toward Major Diseases

Saiful Izwan Abd Razak ✉, Mohd Syahir Anwar Hamzah, Foong Choi Yee, Mohammed Rafiq Abdul Kadir & Nadirul Hasraf Mat Nayan

The stigma of *Crocus sativus*, known as saffron, is one of the most expensive spices in the world. The bioactive components in saffron, picrocrocin, crocin, and safranal, have demonstrated a wide range of uses and capabilities in the medical field. This review is focused on the potential therapeutic applications of saffron on diabetes mellitus (DM), antitumor, anticancer, antidepressant, Alzheimer's disease (AD), cardiovascular disease (CVD), erectile dysfunction and antibacterial effects.

Home / The Natural Products Journal, Volume 6, Number 3



Therapeutic Applications of *Crocus sativus* L. (Saffron): A Review

Authors: Vahedi, Maryam; Govil, Sumit; Kumar, Shailesh; Shrivastava, Divya; Karimi, Roghaye; S. Bisen, Prakash

Source: The Natural Products Journal, Volume 6, Number 3, September 2016, pp. 162-171(10)

Publisher: Bentham Science Publishers

Table 1. Major biological properties (hypolipidaemic, anti-obesity, hypotensive and anti-diabetic) of saffron and its active constituents attributed to its potential effect on metabolic syndrome risk factors

Saffron/compound	Study design	Result	Ref.
Hypolipidaemic			
Saffron	Rats received high fat diet	Improvement in LDL/HDL	32
	STZ-induced diabetic rats	↑HDL, ↓TC, TG, LDL	34
	Healthy rats	↓Serum TC levels	35
	STZ-induced diabetic rats	↓TG, VLDL, ↑adiponectin	39
	Patient with metabolic syndrome	↓Serum HSPs 27, 70 antibody titres	40
Crocin	Rats received high-fat diet	↓TC, TG	32
	STZ-induced diabetic rats	↑HDL, ↓TC, LDL	34
Anti-obesity			
Saffron	Rats received high-fat diet	↓Food consumption	32
	Obese Wistar rats	↓BW, food intake and leptin	45
Crocin	Rats received high-fat diet	↓Rate of body weight gain, total fat pad, weight ratio of epididymal fat to body	32
	Obese Wistar rats	↓Body weight, food intake and leptin	45
Satiereal	Mildly overweight, healthy women	↓Snacking, satiating effect	44
Hypertensive			
Saffron	Normotensive and hypertensive anaesthetised rat	↓MABP	28
	DOCA salt hypertensive rats	↓MSBP	50
	Guinea pig isolated heart	↓Myocardial contractility via calcium channel-blocking effect	52
	Infertile men	↓Mean systolic and diastolic BP	55
	Healthy adult volunteers	↓Standing systolic blood pressure and mean arterial pressures	56
Crocin	Normotensive and hypertensive anaesthetised rat	↓MABP	28
	DOCA salt hypertensive rats	↓MSBP	51
	Rat received diazinon	Modulatory effect of BP	
Saffranal	Normotensive and hypertensive anaesthetised rat	↓MABP	28
	DOCA salt hypertensive rats	↓MSBP	49
Crocetin	Isolated aortic rings	Improve endothelium-dependent ACh relaxations via endothelial NO	53
Anti-diabetic			
Saffron	Healthy male rats	↓FBG, ↑Insulin	35
	Aloxan-induced diabetic rats	↓FBG and HbA _{1c} , ↑insulin	63
	Aloxan-induced diabetic rats	↓FBG, ↑insulin, ↑number of beta cells	64
	C2C12 skeletal muscle cells	↑Glucose uptake and phosphorylation of AMPK/ACC and MAPK	65
Crocin	STZ-induced diabetic rats	↓FBG, TG and VLDL, adiponectin	39
	STZ-induced diabetic rats	↓FBG and AGE products	31
	Aloxan-induced diabetic rats	↓FBG and HbA _{1c} , ↑insulin	63
Saffranal	Aloxan-induced diabetic rats	↓FBG and HbA _{1c} , ↑insulin	63
	C2C12 myotubes	Inhibited PTP1B activity, ↑glucose uptake	66
	Type 2 diabetic KK-Ay mice	Improved impaired glucose tolerance	66
Crocetin	White adipose tissue	Modulatory effect of adiponectin, TNF- α and leptin expression	67



Single kg of saffron spice generates
~63 kg of floral bioresidues.

AZAFRÁN

El azafrán sale de los estigmas del *Crocus sativus*, una planta liliácea oriunda de la zona griega y mediooriental. Su nombre deriva de la palabra árabe *az-zafran*, que designa al color amarillo oscuro; dependiendo de la concentración empleada, el color prestado a la comida o los tejidos (uso antiguo y no desdeñable del azafrán) varía entre el amarillo claro y el rojizo-pardo. Existen otras especies de azafrán, no comestibles. Es la especia más cara del mundo, en razón de la gran cantidad de materia prima precisa para obtener un peso apreciable de ella. No menos de 150.000 flores son necesarias para lograr un kilogramo de estigmas secos. Al tiempo, como pequeñas cantidades son suficientes para los trabajos culinarios, el precio resultante no es tan elevado.



Increasing the Applications of *Crocus sativus* Flowers as Natural Antioxidants

Jéssica Serrano-Díaz, Ana M. Sánchez, Luana Maggi, Magdalena Martínez-Tomé, Luis García-Diz, M. Antonia Murcia, and Gonzalo L. Alonso

Journal of Food Science • Vol. 77, Nr. 11, 2012

Large amounts of floral bio-residues (92.6 g per 100 g of flowers) are generated and wasted in the production of saffron (*Crocus sativus*) spice

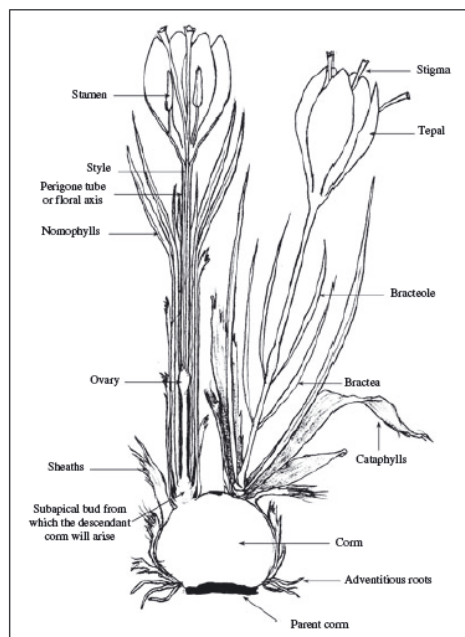
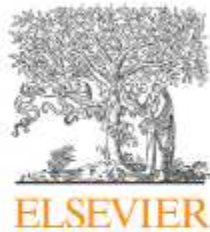


Figure 1—Diagram of the organography of *Crocus sativus* L. (Carmona and others 2006a).

Conclusions

The possible development of new products from *C. sativus* flowers for their antioxidant properties has been shown. The exploitation of whole flowers without separating the stigma could lead to new products with lower production costs than saffron spice. Stamens are the flower parts with the most potent antioxidant activity. Tepals have the highest phenolic content. Floral bio-residues wasted in saffron spice production also show high antioxidant activity. These results suggest that flowers of saffron, floral bio-residues, stigmas, tepals, styles, and specially, stamens are antioxidant sources that may be used as functional ingredients with added value by food and pharmaceutical industries.



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Original Research Article

A contribution to nutritional studies on *Crocus sativus* flowers and their value as food

Jéssica Serrano-Díaz^{a,b}, Ana M. Sánchez^c, Magdalena Martínez-Tomé^b,
Peter Winterhalter^c, Gonzalo L. Alonso^{a,*}

Table 1

Proximate composition (mean \pm SD in g per 100 g on a dry weight, except energy which is expressed in kcal per 100 g on dry weight; $n = 5$) of each freeze-dried part of flowers of saffron (*Crocus sativus* L.), whole flowers and the floral bio-residues from the production of saffron spice.

Material	Moisture	Ash	Proteins	Lipids	Available carbohydrates	Reducing sugars	Energy ^a
Tepals	10.76 \pm 0.24c	6.16 \pm 0.05a	8.17 \pm 0.27a	2.22 \pm 0.29a	64.9 \pm 0.4e	40.3 \pm 1.8d	312.2 \pm 2.2a
Stamens	9.80 \pm 0.32b	11.43 \pm 0.56e	24.05 \pm 0.32f	10.73 \pm 0.38d	33.8 \pm 0.8a	4.3 \pm 1.3a	328.0 \pm 5.4b
Styles	9.86 \pm 0.64b	8.33 \pm 0.07c,d	11.75 \pm 0.37d	3.51 \pm 0.21b	58.6 \pm 1.2b	15.0 \pm 0.9b	313.2 \pm 1.2a
Stigmas	3.84 \pm 0.08a	6.60 \pm 0.66a,b	13.63 \pm 0.12e	8.76 \pm 0.16c	62.0 \pm 0.3d	16.5 \pm 0.9b	381.2 \pm 3.1c
Whole flowers	10.35 \pm 0.56b,c	7.39 \pm 0.12b,c	10.07 \pm 0.24c	3.16 \pm 0.49b	61.2 \pm 0.2c,d	33.0 \pm 0.9c	313.6 \pm 4.2a
Bio-residues	10.78 \pm 0.65c	8.52 \pm 1.18d	9.50 \pm 0.25b	2.82 \pm 0.78a,b	59.9 \pm 0.2b,c	41.5 \pm 1.7d	303.1 \pm 7.0a

Different letters within a column indicate significant statistical differences ($p < 0.05$).

^a Energy was calculated using 4 kcal/g for proteins and available carbohydrates and 9 kcal/g for lipids.

Table 2

Mineral, dietary fiber and soluble sugar composition (mean \pm SD in g per 100 g on dry weight; $n = 5$) of each freeze-dried part of flowers of saffron (*Crocus sativus* L.), whole flowers and the floral bio-residues from the production of saffron spice.

		Tepals	Stamens	Styles	Stigmas	Whole flowers	Bio-residues
Minerals	P	0.232 \pm 0.006a	0.589 \pm 0.022d	0.296 \pm 0.003b	0.327 \pm 0.003c	0.279 \pm 0.010b	0.286 \pm 0.008b
	Mg	0.098 \pm 0.010a	0.309 \pm 0.032c	0.178 \pm 0.012b	0.135 \pm 0.013a,b	0.113 \pm 0.008a	0.160 \pm 0.015b
	Ca	0.125 \pm 0.008a,b	0.216 \pm 0.004c	0.345 \pm 0.016d	0.107 \pm 0.012a	0.139 \pm 0.002b	0.467 \pm 0.012e
	Fe	0.028 \pm 0.001d	0.024 \pm 0.001c	0.035 \pm 0.001e	0.011 \pm 0.001a	0.016 \pm 0.001b	0.016 \pm 0.001b
	K	1.353 \pm 0.010a	3.796 \pm 0.031c	1.816 \pm 0.078b	1.486 \pm 0.037a	1.395 \pm 0.061a	1.735 \pm 0.051b
	Na	0.012 \pm 0.001a,b	0.011 \pm 0.001a	0.019 \pm 0.001c	0.010 \pm 0.001a	0.010 \pm 0.001a	0.014 \pm 0.001b
Dietary fiber	Total DF ^a	27.5 \pm 0.1e	32.3 \pm 0.1f	18.5 \pm 0.1c	13.8 \pm 0.1a	14.4 \pm 0.1b	25.1 \pm 0.1d
	Insoluble DF ^a	8.6 \pm 0.1c	21.1 \pm 0.1f	16.1 \pm 0.1e	7.8 \pm 0.1b	5.9 \pm 0.1a	13.8 \pm 0.1d
	Soluble DF ^a	18.9 \pm 0.1e	11.2 \pm 0.1d	2.4 \pm 0.1a	6.0 \pm 0.1b	8.5 \pm 0.1c	11.3 \pm 0.1d
	Insoluble/soluble DF ^a	0.5 \pm 0.0a	1.9 \pm 0.0e	6.7 \pm 0.0f	1.3 \pm 0.0d	0.7 \pm 0.0b	1.2 \pm 0.0c
Soluble sugars	Glucose	11.59 \pm 0.62e	5.60 \pm 0.57a	8.26 \pm 0.18b,c	7.40 \pm 0.01b	9.62 \pm 0.99c,d	10.30 \pm 0.70d,e
	Fructose	0.53 \pm 0.01a	1.31 \pm 0.01b	0.56 \pm 0.01a	0.39 \pm 0.01a	1.38 \pm 0.09b	0.48 \pm 0.01a
	Sucrose	0.22 \pm 0.01b	n.d.	n.d.	n.d.	0.16 \pm 0.01a	0.09 \pm 0.01a
	Maltose	0.14 \pm 0.01b	n.d.	0.06 \pm 0.01a	n.d.	0.07 \pm 0.01a	0.06 \pm 0.01a
	Inositol	0.26 \pm 0.01b	0.71 \pm 0.01d	n.d.	0.33 \pm 0.01c	0.15 \pm 0.01a	0.15 \pm 0.01a
	Sorbitol	n.d.	0.10 \pm 0.01a	n.d.	0.20 \pm 0.02b	n.d.	n.d.
	Mannitol	0.72 \pm 0.01b	n.d.	n.d.	n.d.	0.95 \pm 0.06c	0.49 \pm 0.03a

Different letters in each row indicate significant statistical differences ($p < 0.05$).

^a DF, dietary fiber; n.d., not detected.

Table 3

Mean percentage of satisfaction for Dietary Reference Intakes (DRIs, s.a.) of nutrients for 19–30 year old men by consumption of 100 g of each freeze-dried part of flowers of saffron (*Crocus sativus* L.), whole flowers and the floral bio-residues from the production of saffron spice.

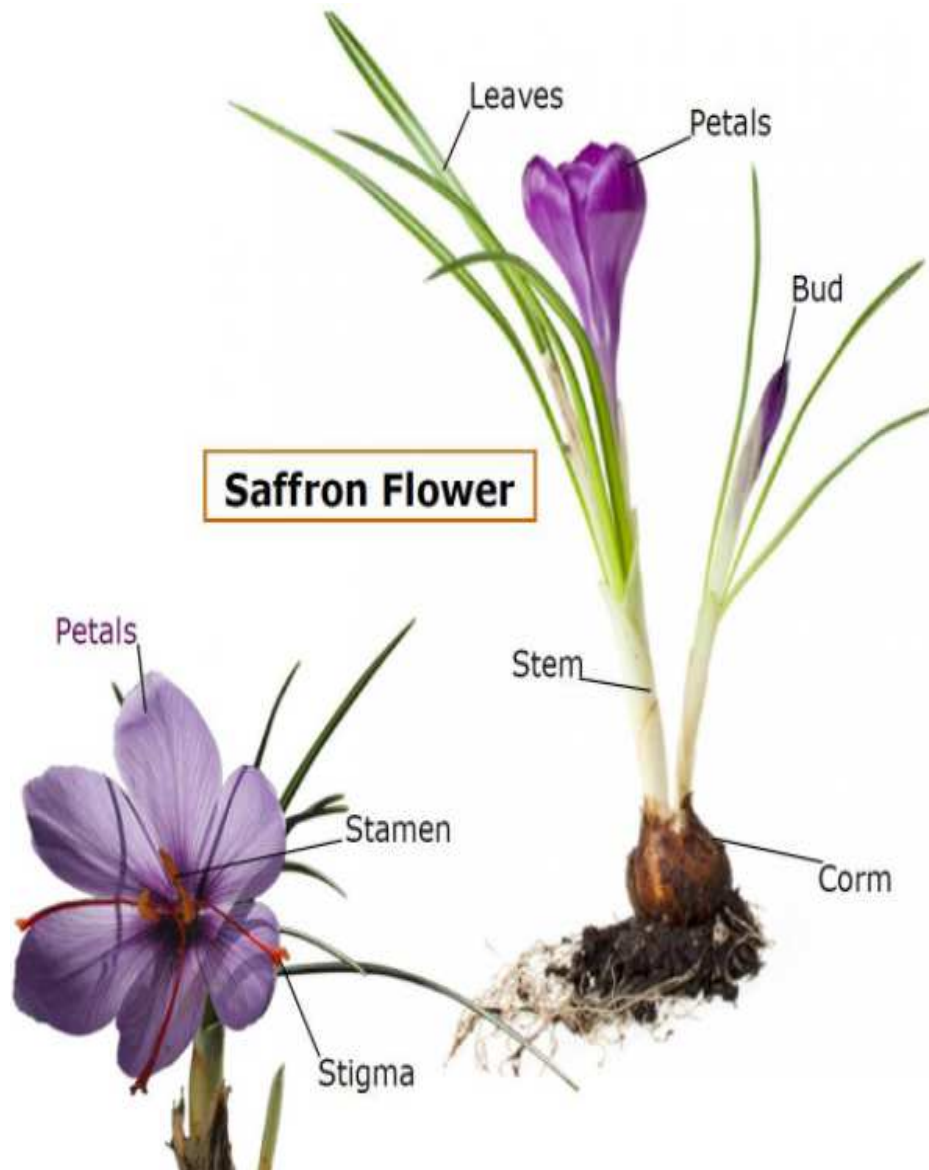
Material	Proteins ^a	Lipids ^b	Carbohydrates ^a	Total DF ^{c,d}	P ^a	Mg ^a	Ca ^a	Fe ^a	K ^c	Na ^c
Tepals	14.6	8.1	49.9	72.4	33.1	31.3	9.8	350.0	28.8	0.8
Stamens	42.9	39.0	26.0	85.0	84.1	54.1	30.9	303.8	80.8	0.7
Styles	21.0	12.8	45.1	48.7	42.3	86.2	17.8	433.8	38.6	1.3
Stigmas	24.3	31.9	47.7	36.3	46.7	26.7	13.5	141.3	31.6	0.7
Whole flowers	18.0	11.5	47.1	37.9	39.8	34.7	11.3	200.0	29.7	0.7
Bio-residues	17.0	10.3	46.1	66.1	40.9	116.8	16.0	200.0	36.9	0.9

^a Recommended Dietary Allowances (RDAs).

^b Acceptable Macronutrient Distribution Range (AMDRs).

^c Adequate Intakes (AIs).

^d DF, dietary fiber.



Phytochemical analysis and antioxidant activity of different tissue types of *Crocus sativus* and oxidative stress alleviating potential of saffron extract in plants, bacteria, and yeast



Shoib Ahmad Baba ^{a,c}, Aubid Hussain Malik ^{a,c}, Zahoor Ahmed Wani ^{a,c}, Tabasum Mohiuddin ^{a,c}, Zeeshan Shah ^b, Nazia Abbas ^a, Nasheeman Ashraf ^{a,*}

Table 1

Total phenolic total flavonoid and carotenoid content of different tissues of *Crocus sativus*.

Tissue sample	Extract	Total phenolic content ¹ (mg/g)	Total flavonoid content ² (mg/g)	Total carotenoid content (µg/g)
Stigma	Ethanollic	8.28 ± 0.56	3.53 ± 0.11	546.55 ± 25.17
	Aqueous	6.54 ± 0.61	3.61 ± 0.32	
Leaf	Ethanollic	5.62 ± 0.60	1.61 ± 0.12	171.12 ± 13.12
	Aqueous	4.26 ± 0.37	2.00 ± 0.20	
Corm	Ethanollic	7.07 ± 0.62	2.46 ± 0.28	045.64 ± 4.85
	Aqueous	5.97 ± 0.22	2.56 ± 0.25	

Values are means of three biological replicates.

¹ mg gallic acid equivalent (GAE)/g DW.

² mg rutin equivalent/g DW.

The results demonstrate that *C. sativus* stigma, corms, and leaves may act as excellent sources for isolation of potential antioxidants and with significant amounts of carotenoids, they may serve as natural antioxidants in foods, beverages, drinks, and pharmaceutical preparations.



Obesidad
Hipertensión
Antibacteriano
Úlceras
Antioxidante
Diabetes
Anticancerígeno
Alzheimer
Afrodisíaco

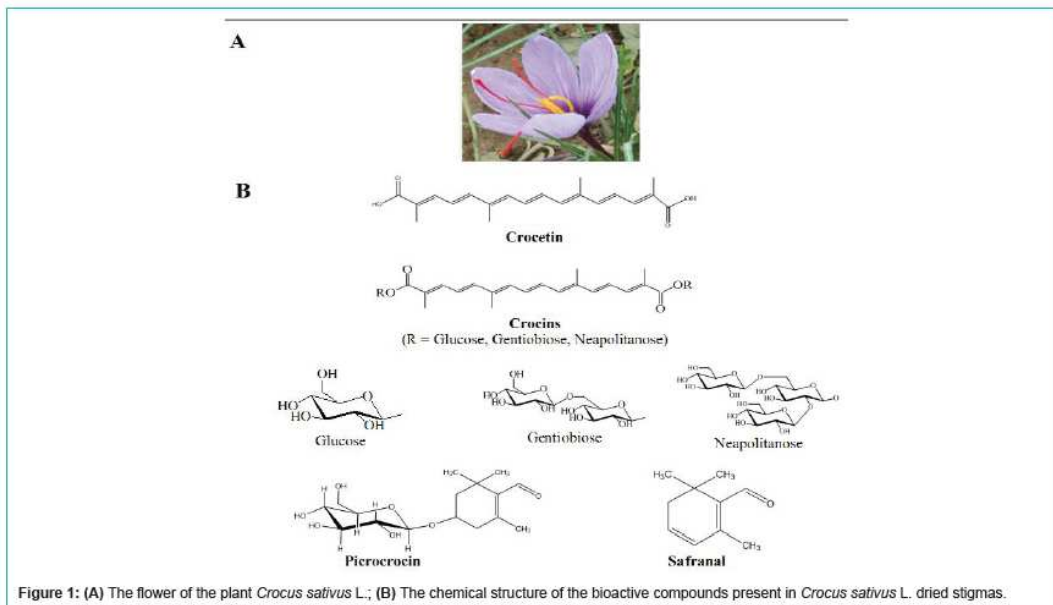
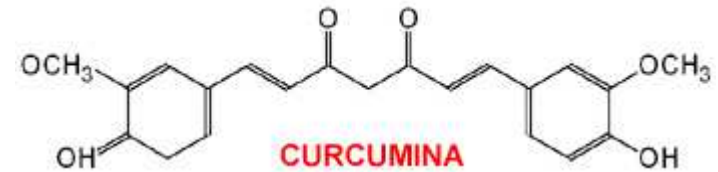


Table 3 Human equivalent doses calculated for the different saffron animal studies.

Effects	Reference	Animal	Saffron product	Frequency	Saffron equivalent doses (mg/kg b.w.) ^a	HED (mg/person) ^b
Biological activities						
Antioxidant	Hosseinzadeh <i>et al.</i> 2007b	Rats	Ethanollic extract	Mono dose	5 - 80	57 - 908
			Crocin		172 - 1379	1 957 - 15 657
			Safranal		14 505 - 72 523	164 646 - 823 229
Ulcers	Al-Mofleh <i>et al.</i> 2006	Rats	Extract	Mono dose	250	2 838
	Kianbakht and Mozaffari 2009	Rats	Extract		25 - 250	284 - 2 838
			Crocin		8 - 35	88 - 391
			Safranal		362 613 - 725 225	4 116 144 - 8 232 286
Nervous system damage						
Neuronal injury	Hosseinzadeh and Sadeghnia 2005	Mice	Safranal	Mono dose	109 234	1 239 956
Retinal function	Maccarone <i>et al.</i> 2008	Rats	Extract	Mono dose	1	11
Parkinson	Ahmad M <i>et al.</i> 2005	Rats	Crocin	Daily, 7 days	0.3	3
Seizures	Hosseinzadeh and Khosravan 2002	Mice	Ethanollic extract	Mono dose	0.2 - 2	1 - 11
			Aqueous extract		0.1 - 0.8	0.45-5
	Hosseinzadeh and Talebzadeh 2005	Mice	Safranal		21 757 - 50 766	123 484 - 288 130
	Hosseinzadeh and Sadeghnia 2007	Rats	Safranal		10 923 - 43 694	123 996 - 495 982
Learning behaviour	Pitsikas and Sakellaris 2006	Rats	Extract	Mono dose	30 - 60	341 - 681
	Pitsikas <i>et al.</i> 2007	Rats	Crocin	Daily	52 - 103	587 - 1 174
Anxiety	Pitsikas <i>et al.</i> 2008	Rats	Crocin	Mono dose	172	1 957
	Hosseinzadeh and Noraei 2009	Mice	Extract		56 - 560	318 - 3 178
			Safranal		21757 - 50 766	123 484 - 288 130
Sedative/relaxant	Hosseinzadeh and Ghenaati 2006	Guinea pigs	Ethanollic extract	Mono dose	100 - 800	1 514 - 12 108
			Safranal		36 261 - 108 784	548 819 - 1 646 457
Depression	Karimi <i>et al.</i> 2001	Mice	Safranal	Mono dose	23 - 75	128 - 426
			Crocin		172 - 2 079	979 - 11 743
	Hosseinzadeh <i>et al.</i> 2004	Mice	Aqueous extract		160 - 320	908 - 1 816
			Ethanollic extract		200 - 800	1 135 - 4 541
Cardiovascular injury						
Atherosclerosis	Sheng <i>et al.</i> 2006	Rats	Crocin	Daily, 10 days	86 - 1 250	979 - 14 189
	Asqad <i>et al.</i> 2009	Rats	Extract	Daily, 5 days	25 - 100	284 - 1 135
Myocardial infarction	Goyal <i>et al.</i> 2009	Rats	Crocin	Daily, 21 days	69	783
	Yan <i>et al.</i> 2010	Rats	Crocin		172	1957
Pheripheral vascular diseases	Yang <i>et al.</i> 2008	Rats	Crocin	Daily, 2 days	86 - 625	979 - 7 095
Insulin resistance	Xi <i>et al.</i> 2007	Rats	Crocin	Daily, 8 weeks	69 - 138	783 - 1 566
Cancer and tumours						
Cancer and tumours	Premkumar <i>et al.</i> 2006	Mice	Extract	Daily, 5 days	20 - 80	114 - 454
Skin cancer	Das <i>et al.</i> 2009	Mice	Extract	Daily, 7 days	200	1 135
Pancreatic cancer	Dhar <i>et al.</i> 2009	Mice	Crocin	Daily, 30 days	14	78
Lung cancer	Magesh <i>et al.</i> 2006	Mice	Crocin	Daily, 4 weeks	69	391
Antinociceptive effects						
Antinociceptive	Hosseinzadeh and Shariaty 2007	Mice	Safranal	Mono dose	14 505 - 72 522	82 323 - 411 614
Sexual behaviour dysfunction						
Sexual behaviour dysfunction	Hosseinzadeh <i>et al.</i> 2008	Rats	Extract	Mono dose	80 - 320	908 - 3 632

^a Doses were converted to mg/kg b.w. of saffron equivalent, taking into account a saffron humidity of 9%, 0.66% safranal content and 32% on dry basis of crocetin content

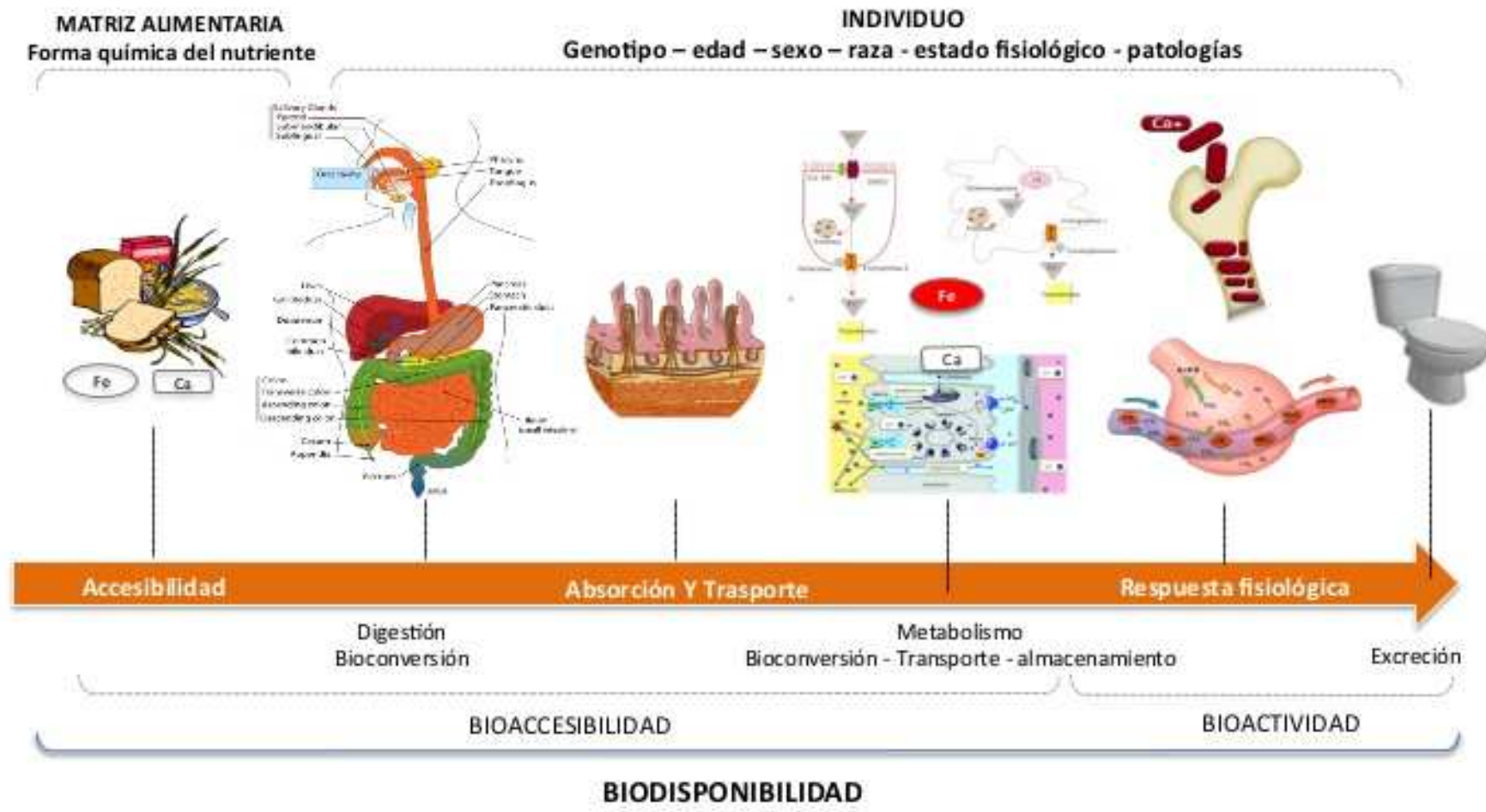
^b HED were calculated using K_m factors based on BSA. The final HED was multiplied by a body weight of 70 kg



Potential Healthy Effects of Saffron Spice (*Crocus sativus* L. Stigmas) Consumption

Carmen Licón¹ • Manuel Carmona¹ • Silvia Llorens¹ •
María Isabel Berruga¹ • Gonzalo L. Alonso²

BIODISPONIBILIDAD



Bioavailability of Curcumin: Problems and Promises

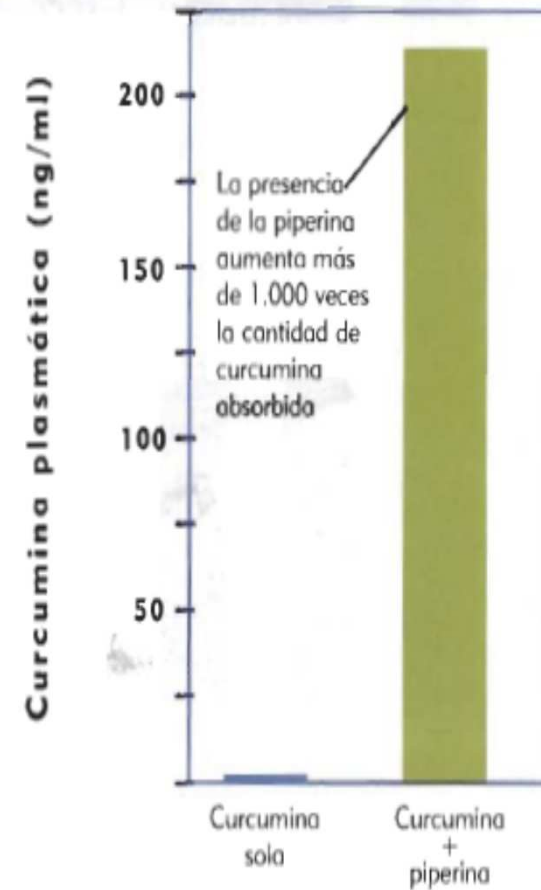
Preetha Anand[†], Ajaikumar B. Kunnumakkara[†], Robert A. Newman[‡] and Bharat B. Aggarwal^{††}

Cytokine Research Laboratory and Pharmaceutical Development Center, Department of Experimental Therapeutics, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030

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EJEMPLO DE SINERGIA INDIRECTA



Intestinal formation of trans-crocetin from saffron extract (*Crocus sativus* L.) and in vitro permeation through intestinal and blood brain barrier.

Lautenschläger M¹, Sendker J¹, Hüwel S², Galla HJ², Brandt S¹, Düfer M³, Riehemann K⁴, Hensel A⁵.

Abstract

AIMS: Extracts of saffron (*Crocus sativus* L.) have traditionally been used against depressions. Recent preclinical and clinical investigations have rationalized this traditional use. Trans-crocetin, a saffron metabolite originating from the crocin apocarotenoids, has been shown to exert strong NMDA receptor affinity and is thought to be responsible for the CNS activity of saffron. Pharmacokinetic properties of the main constituents from saffron have only been described to a limited extent. Therefore the present in vitro study aimed to determine if crocin-1 and trans-crocetin are able to pass the intestinal barrier and to penetrate the blood brain barrier (BBB). Additionally, the intestinal conversion of glycosylated crocins to the lipophilic crocetin had to be investigated. Experiments with Caco-2 cells and two different porcine BBB systems were conducted. Further on, potential intestinal metabolism of saffron extract was investigated by ex vivo experiments with murine intestine.

METHODOLOGY: In vitro Caco-2 monolayer cell culture was used for investigation of intestinal permeation of crocin-1 and trans-crocetin. In vitro models of porcine brain capillary endothelial cells (BCEC) and blood cerebrospinal fluid barrier (BCSFB) were used for monitoring permeation characteristics of trans-crocetin through the blood brain barrier (BBB). Intestine tissue and feces homogenates from mice served for metabolism experiments.

RESULTS: Crocin-1, even at high concentrations (1000 μ M) does not penetrate Caco-2 monolayers in relevant amounts. In contrast, trans-crocetin permeates in a concentration-independent manner (10-114 μ M) the intestinal barrier by transcellular passage with about 32% of the substrate being transported within 2 h and a permeation coefficient of $P_{app} 25.7 \times 10^{-6} \pm 6.23 \times 10^{-6}$ cm/s. Trans-crocetin serves as substrate for pGP efflux pump. Trans-crocetin permeates BBB with a slow but constant velocity over a 29 h period (BCEC system: $P_{app} 1.48 \times 10^{-6} \pm 0.12 \times 10^{-6}$ cm/s; BCSFB system $P_{app} 3.85 \times 10^{-6} \pm 0.21 \times 10^{-6}$ cm/s). Conversion of glycosylated crocins from saffron extract to trans-crocetin occurs mainly by intestinal cells, rather than by microbiological fermentation in the colon.

CONCLUSION: The here described in vitro studies have shown that crocins from saffron are probably not bioavailable in the systemic compartment after oral application. On the other side the investigations clearly have pointed out that crocins get hydrolyzed in the intestine to the deglycosylated trans-crocetin, which subsequently is absorbed by passive transcellular diffusion to a high extend and within a short time interval over the intestinal barrier. Crocetin will penetrate in a quite slow process the blood brain barrier to reach the CNS. The intestinal deglycosylation of different crocins in the intestine is mainly due to enzymatic processes in the epithelial cells and only to a very minor extent due to deglycosylation by the fecal microbiome. On the other side the fecal bacteria degrade the apocarotenoid backbone to smaller alkyl units, which do not show any more the typical UV absorbance of crocins. As previous studies have shown strong NMDA receptor affinity and channel opening activity of trans-crocetin the use of saffron for CNS disorders seems to be justified from the pharmacokinetic and pharmacodynamic background.



COMPUESTOS BIOACTIVOS DE INTERÉS EN EL AZAFRÁN DE LA MANCHA



¡Muchas gracias
por su atención!



Dr. José Miguel Soriano del Castillo



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