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THE MOSS REPORTS

In our increasingly technologically driven world it is easy to overlook the low-tech solutions that are sometimes right in front of us. While no one would deny the benefits that technological sophistication has brought to the practice of medicine, it is also extremely important to use our growing scientific capabilities to investigate the ways in which inexpensive, naturally occurring substances might be harnessed in the service of helping sick people.

This week I discuss the potential medicinal uses of saffron, a spice harvested from a member of the humble crocus family. Could this spice, cherished by civilizations ancient and modern, hold as yet untapped benefits in the treatment and prevention of cancer? A growing number of respected scientists believe that yes, it could.

For the past thirty years I have been studying the field of cancer therapy and prevention, monitoring developments in the world of oncology, helping cancer patients and their families weigh up the benefits and drawbacks of treatments both conventional and alternative. As a product of these long years of research I have written *The Moss Reports*, a series of more than two hundred individual reports on different kinds of cancer.

If you or someone you love has received a diagnosis of cancer, a *Moss Report* can provide you with the key to understanding the best that conventional and alternative medicine have to offer. You can order a *Moss Report* on your specific cancer type by calling **Diane** at **1-800-980-1234** (814-238-3367 from outside the US), or by visiting our website: <http://www.cancerdecisions.com>

We look forward to helping you.

WELCOME TO SAFFRONOLOGY

"I'm just wild about Saffron," sang Donovan, in his 1967 hit "Mellow Yellow." Saffron in that popular song was not a spice but a girl (who, if my memory serves me well, was equally wild about Donovan). However, the sentiment is turning out to be predictive of a different kind of "flower power" than we ever envisioned during the Summer of Love. This is the power of the garden crocus - or more specifically its three bright-red stigmas - from which saffron is derived.



Pictured above: Crocus

The health-conscious public may turn out to be "wild about saffron," too, at least if Dr. Fikrat I. Abdullaev has his way. According to this innovative researcher from the former Soviet republic of Azerbaijan, as well as a growing cohort of like-minded scientists, the world's most expensive culinary ingredient may also be recognized as one of the most healthful. It holds promise against a host of diseases, including cancer.

Dr. Abdullaev currently heads a team of nine at the National Institute of Pediatrics in Mexico City. He also holds an appointment at the Laboratory of Genome Biochemistry of the Institute of Botany, Azerbaijan Academy of Sciences, where he received his PhD in 1970. He has another doctorate from the Ukrainian Academy of Science in Kiev. From 1990-1993 he was a visiting scientist at Rutgers University in New Jersey. Dr. Abdullaev is the author of over 120 scientific papers and abstracts, and several patents. He is fluent in many languages and is thus ideally positioned to lead an international investigation into saffron's medicinal properties.



Pictured above: Dr. Abdullaev's research team in front of the National Institute of Pediatrics

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A Traditional Medicine

The word 'saffron' is found in recognizable form in even the most ancient languages. The medicinal use of saffron dates back to ancient times and is mentioned in the works of Hippocrates, Galen and the other great clinicians. Some of the many traditional uses of saffron include the treatment of cough, flatulence, stomach disorders, insomnia, uterine bleeding, scarlet fever, colds, and cardiovascular disease. Today, however, it is best known as a flavoring and colorant in various foods: Spanish paella, Italian risotto, French bouillabaisse, Mexican fiambre, Arabic lamb and chicken dishes, Iranian plov, Azerbaijani pakhlava, and Indian desserts and sauces. It is also found in Swedish, Cornish and Pennsylvania Dutch holiday breads.

The intense orange color of saffron is a hint as to its medicinal nature. It is particularly rich in carotenoids, which are antioxidants that protect the body from free radical damage. But despite its impeccable credentials as an antioxidant, saffron has until recently gotten little scientific recognition as a potential source of new medicines.

That may soon change. Dr. Abdullaev and Dr. Jose Antonio Fernandez of Spain co-chaired the First International Symposium on Saffron Biology and Biotechnology, held in Albacete, Spain in October, 2003. This historic meeting was organized under the auspices of the International Society for Horticultural Science (ISHS) and drew about 90 participants from

20 countries. The proceedings of that symposium were recently published as ISHS's Acta Horticulturae 650.

Click or go here to see a description of ISHS Acta Horticulturae 650:

<http://www.actahort.org/books/650/>

Saffron contains over a hundred components, but the three most interesting appear to be:

Crocin, which is responsible for saffron's orange color

Picrocrocin, which is responsible for its bitter taste; and

Safranal, which is responsible for its odor and aroma.

Although in his home town of Baku, Azerbaijan, Dr. Abudallaev worked on various natural and synthetic substances, his main interest since the 1980s has been the "extremely promising strategy" of chemoprevention. (Despite the presence of the forbidding prefix 'chemo-' in that word, chemoprevention does not refer to chemotherapy, but to the use of natural or synthetic substances, alone or in combination, to prevent the development of diseases such as cancer.)

Saffron is produced from the dried stigmas (which are the pollen-receiving parts of the flower) of *Crocus sativus* L. This blue-violet crocus is actually a member of the Iris family. Commercially, saffron is mainly cultivated in Iran, but also in Dr. Abdullaev's native Azerbaijan, France, Greece, India, Italy, Spain, China, Israel, Morocco, Turkey, Egypt and Mexico.

Saffron is not always what it appears to be: there are also some false (i.e., non-crocus derived) versions on the market. For example, Indian safflower, *Carthamus tinctorius* L., a member of the daisy family, or Compositae, is lighter red than true saffron, but is sometimes used to adulterate the real thing. In ancient, as well as modern, times adulteration has been a problem. Medieval folk took saffron adulteration very seriously: there are historical records of 15th century saffron scammers being burned in the market-place along with their adulterated saffron. On another occasion three persons convicted of the same crime were buried alive, according to an informative article on saffron in the 1911 Encyclopaedia Britannica.

One must also make sure not to confuse saffron with an entirely different plant called meadow saffron (*Colchicum autumnale*). This species also has medicinal uses, but unlike true saffron, meadow saffron can be very poisonous and should be strictly avoided by would-be herbalists.

Saffron is not only used as a food flavoring and colorant, but as a dye for clothing, especially in underdeveloped countries. It is so intensely colorful that one grain of powdered saffron imparts a distinctly yellow tint to ten gallons of water. Saffron-robed priests are a common sight in India and saffron is the chosen color of the Hindu nationalist parties in India.

Despite its popularity as a culinary spice in so many countries, Americans rarely use saffron in their cooking, perhaps because of its great cost. One gram of saffron (i.e., 1/28th of an ounce) costs around \$10 in US supermarket. The main reason for saffron being so expensive is that it is still cultivated and harvested by hand, as it has been for several millennia, and it takes over 200,000 of the stigmas, obtained from 70,000 flowers, to yield one pound of true saffron.



Pictured above: A traditional saffron harvesting

Is Saffron Toxic?

Perhaps because of a mistaken association with the poisonous meadow saffron, *Colchicum autumnale*, saffron has an ill-deserved reputation as being somewhat toxic, but Dr. Abdullaev has established that saffron is safe when taken in dietary amounts. He has shown that oral administration of saffron extract at concentrations from 0.1 to 5 grams per kilogram of body weight (g/kg) is nontoxic in mice (Abdullaev F, et al., unpublished data). Saffron has also been shown to be non-mutagenic (i.e., it does not cause mutations).

Animal studies indicated that the orally-administered amount that kills half the tested animals (the so-called LD50) was 20.7 grams per kilogram. A dose of 5 grams per kilogram would be the equivalent to a 165 pound human eating up 13.4 ounces at one sitting. There is only one circumstance known to me in which this unlikely scenario has happened. Saffron has a folk reputation for bringing an end to an unwanted pregnancy. There is no evidence to support the effectiveness of this method, but ethnobotanist James Duke, PhD, has reported that fatalities have occurred from overdoses taken for this purpose. However, in the relatively small quantities in which saffron has been consumed for millennia, it seems a perfectly safe substance.

Effects on Cancer

What will interest most readers, of course, is the possible therapeutic effect of saffron on cancer. And, indeed, a growing body of laboratory evidence indicates that saffron does have anticancer effects. The anticancer potential of saffron was first pointed out in papers by the Indian scientist S.C. Nair in 1991. Dr. Abdullaev confirmed and extended Nair's findings the following year. Later, scientists from Greece (Petros A. Tarantilis in 1994) and Spain (Julio A. Escribano in 1996) supported these results. In the last decade, research on saffron's antitumor effects has been published in about 40 experimental and review articles. Just as saffron is produced in many parts of the world, so anticancer research on saffron is also a multinational effort, and involves scientists from Azerbaijan, Greece, Hungary, India, Japan, Mexico, Spain, USA and other countries.

For instance, extracts of saffron have been shown to inhibit the formation of tumors and/or to retard tumor progression in a variety of experimental animal systems. The topical application of a saffron extract has been shown to inhibit both the initiation and the promotion of cancer by a common carcinogen, DMBA, which is used to induce skin cancer for experimental purposes. Researchers found that feeding a saffron extract prevented the formation of soft tissue sarcomas in mice. Most excitingly, saffron extracts have been shown to significantly prolong - by almost three-fold - the life spans of mice undergoing experimental chemotherapy with the toxic anticancer drug, cisplatin. They also partially prevented the decrease in body weight, hemoglobin levels, and leukocyte counts associated with that form of chemotherapy (Nair 1991).

Another study showed that when saffron was combined with two other substances, the amino acid cysteine and the antioxidant vitamin E, it had a protective effect against the toxicity of cisplatin. Together, these three protective agents significantly reduced blood urea nitrogen, serum creatinine and blood glucose levels, as well as reducing many other harmful chemical changes in the body (el Daly 1998). Taken together, these studies indicate that saffron (with or without other substances, such as antioxidants or their precursors) has the potential to alleviate the toxicity of cisplatin, including the nephrotoxicity (damage to the kidneys) that is one of cisplatin's most serious side effects. This potential use of saffron has gone largely unexplored by conventional oncology since it was first pointed out in 1991. In fact, a search of all abstracts from the American Society of Clinical Oncology (ASCO) meetings of the last 11 years turns up hundreds of papers on cisplatin toxicity, but not a single one that even mentions the word 'saffron' or 'crocus'. It is an astonishing omission, considering the damage that platinum-containing drugs such as cisplatin can do.

In other studies, S. C. Nair and colleagues showed that the oral administration of saffron extract inhibited the growth of mouse tumors that were derived from three different kinds of cancer cells (S180, DLA and EAC), and significantly increased (again by two- to three-fold) the life spans of treated tumor-bearing mice (Nair 1997b).

Later, these same Indian authors reported that giving saffron by mouth to lab animals significantly slowed the growth of two different kinds of cancer cells (DLA and S-180). The

authors suggested that the increased levels of carotenes and vitamin A may have accounted for this anticancer effect.

Interestingly, when saffron extract was encapsulated with lipids and then injected into the mice, there was an increase in the antitumor effect of this extract towards several solid tumors, including EAC tumor cells that had formerly been insensitive to orally administered saffron extract (Nair 1992).

In 1999, Spanish scientists reported that crocin, one of the carotenoids isolated from saffron, increased the survival time and decreased the growth of colon cancer in female rats, without however having any significant effects on the tumors in male animals. This raised the possibility that the selective antitumor action of crocin in female rats might be modulated by some as yet unidentified hormonal factor (Garcia-Olmo 1999).

Dr. Abdullaev and his colleagues have also found that naturally occurring saffron extract, in combination with two synthetic compounds, sodium selenite or sodium arsenite, may have a synergistic effect with saffron and might therefore have an important role in cancer chemoprevention (Riverón-Negrete 2002).

How might saffron exert these effects? Some test tube (in vitro) studies with human malignant cells have shown that saffron inhibits the synthesis of nucleic acid (DNA or RNA) in cancer cells but has no effect on overall protein synthesis (Abdullaev 1992a and Abdullaev 1992b). It has also been observed that saffron increases the intracellular levels of a substance called reduced glutathione as well as glutathione-related enzymes. This suggests a possible antioxidant activity for this herbal compound.

Dr. Abdullaev has suggested that saffron and its constituents be tried clinically as "alternative anticancer agents, which alone and in combination with other synthetic substances may have the potential for the prevention and the treatment of certain forms of cancer" (Abduallev 2002). Because the relationship between saffron and cancer is an important concern, he says, comprehensive, in-depth studies need to be conducted. He suggests the following four initial research projects:

- Define the mechanism or mechanisms involved in the therapeutic properties of saffron
- Investigate the mechanisms involved in saffron cancer chemoprevention
- Determine the biologically active components of saffron
- Perform human studies to define efficacy of saffron in cancer treatment and prevention

Of course, the scarcity and relative expense of saffron may pose an obstacle to prevention or treatment trials using this agent. This underscores the need to develop indoor cultivation methods in order to achieve the highest quality of saffron at the lowest possible price. The results of current research provide the scaffolding to construct a platform for a new scientific discipline that Dr. Abdullaev calls 'saffronology.' With the publication of the proceedings of the First International Conference on saffron we expect to hear a lot more about this emerging discipline.

Practical Considerations

If readers want to increase their own intake of saffron there are many places to obtain it. However, the local supermarket is not the best place. You may be shocked to see how few strands you get in a standard bottle. And besides, since it is so expensive and still so relatively unknown, the stock at the supermarket may not be the freshest. The brand I myself use is "The Gathering of Saffron", imported from La Mancha, Spain. It consists of whole strands (i.e., it is not powdered). However, much of the saffron coming out of Spain actually originates in Iran, the world's number one producer.

One ounce of saffron can generally be found on the Internet for between \$30 and \$40. The redder the saffron, generally, the more potent it will be. If you are lucky enough to have an ethnic specialty grocery store nearby, you may obtain it even more cheaply. A little goes a long way. I paid just \$20 for an ounce of saffron in the Indian neighborhood of Jackson Heights, New York. That was three years ago and although I use saffron liberally I still have a little left.

Saffron is a promising agent and Dr. Abdullaev is a tireless proponent of its virtues. So there will undoubtedly be many new developments in this field. I will keep readers apprised of the unfolding of the colorful field of saffronology.

--Ralph W. Moss, Ph.D.



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