

Zataria Multiflora: Iran

Abbas Shafiee
Faculty of Pharmacy
Tehran University of Medical Sciences
Tehran, Iran

Summary

Zataria multiflora is a thyme-like plant that grows wild in central and southern Iran. It is a member of the Lamiaceae family to which mint, rosemary and several other medically useful plants also belong. In Iran, *Zataria multiflora* is used in traditional folk remedies for its antiseptic, analgesic (pain-relieving) and carminative (anti-flatulence and intestine-soothing) properties. Despite its impressive array of medical applications, little research had been carried out on the volatile constituents of this plant — the physical and chemical dimensions that make it behave the way it does.

That is why when the Faculty at Tehran University of Medical Sciences in Iran commenced a project to assess *Zataria multiflora* as a wild plant for medical use in 1994, it began by analyzing the essential oil of the plant's aerial parts — the parts that grow above the ground. The essential oil is obtained by distilling or pressing the plant's leaves, roots, fruits, seeds, stems and/or flowers. Basically, the essential oil contains the plant's "essence" — a complex chemical that provides its smell and other properties, including those that make it medically useful.

Once scientists had studied the oil, they measured and recorded its antimicrobial activity (its ability to kill off microbes). *Zataria multiflora* was found to perform well in terms of containing adequate quantities of effective active chemicals that could be used in pharmacology to produce medicines. On the basis of these findings and in collaboration with the Tolid Dara Pharmaceutical Company, the project team has developed two drug formulations: (1) broncho TDA syrup, an expectorant and cough suppressant, and (2) an antimicrobial and antifungal mouth wash. In addition, a vaginal douche and pain-relieving cream are currently under development.

Background and Justification

People throughout the world have become increasingly concerned about the sometimes dramatically adverse side-effects of synthetic, human-made chemicals in medicines. As a result, there is a growing movement to find new, or rediscover old, ways of treating illness and improving general health.

This project was a response to those concerns, as pharmacologists at Tehran Medical School searched for potential alternatives largely by turning their attention to local medicinal plants. Among these plants are several species of the genus *Thymus* (thyme), including *Zataria multiflora*, that was already well-known to folk healers. The findings of the university team's research were encouraging, both for what they discovered about the particular plant and for justifying similar studies into other traditional plant cures. The project, in fact, proved that industry can be encouraged to use plant ingredients when those ingredients have been analyzed and assessed in detail by reputable and respected institutions.

Although *Zataria multiflora* had been used in traditional medicine, it had never been an ingredient of industrially produced drugs until the project findings established its scientifically-based credentials. Conventional doctors and the pharmaceutical industry have become far more confident about some of the medically beneficial ingredients of this plant, particularly as an alternative to synthetic expectorants and cough suppressants.

Description

During the project, microbiologists identified, analyzed, disassembled and measured *Zataria multiflora's* essential oil from four regions of Iran. Findings from each of these regions — including the different varieties that grow there and both fresh and dried plants — were compared so that the best plant variety and growing conditions could be determined. In general, the oil was found to contain significant amounts of the substances thymol (48.4 percent) and carvacrol (12.6 percent), both of which are antimicrobial and

antifungal. After these and other useful properties of the oil's ingredient were studied, it was decided that the plant could best be used in medicine as an antiseptic, analgesic and cough suppressant.

Oils of *Zataria multiflora* strains that contain particularly large quantities of thymol and carvacrol are used in mouthwashes, while oils from the best-quality plant variety are used in an expectorant and cough suppressant formula. Oils from some of the regions and varieties studied were also found to kill microbes that can cause a wide range of diseases and conditions, including vaginal, urinary tract (*Escherichia coli*) and yeast (*Candida albicans*) infections. As a result, a vaginal douche and analgesic cream, containing *Zataria multiflora* oil extracts, are currently being developed and will soon be available. Finally, the oil was also found to be useful in the crystallization of menthol for use in the food, flavourings and cosmetic industries.

Partnerships

Partnerships and collaborations between academies and the private sector were keys to success. Chemistry, pharmacogony and pharmacology researchers from the university worked closely, effectively and productively with colleagues from a private pharmaceutical company, creating an atmosphere in which technological innovations, research and development activities, sharing and dispersion of information, training of personnel and commercialization all ran smoothly. Thanks to this cooperation between academia and industry, a part of Iran's folk culture is now being confidently produced and marketed on a modern commercial scale.

Patenting and Commercialization

No patents have yet been filed for the products developed.

Replicability

Local wild plants are used in traditional medicines, fragrances, food ingredients, cosmetics and other products in many countries across the developing and developed world. This project shows how modern science is able to find new ways of using such plants through careful research and study combined with innovation and business acumen. Similar activities could be carried out elsewhere to find new (or support old) ways of making the most of natural, readily available ingredients.

Lessons Learned

The study of traditional medicines could lead to the development of new formulations and the discovery of basic compounds for use in modern medicine.

Collaboration among many different branches of scientific, pharmaceutical and medical research is essential for success.

For example, once the chemical make-up of *Zataria multiflora* essential oil had been discovered by a microbiologist, the medical benefits of those chemicals had to be tested. At this point, a pharmacologist joined the team, and laboratory rats were studied to determine the effectiveness of both the plant's oils and its hydroalcoholic extracts as anti-inflammatories.

The project team then began to explore ways of applying their new knowledge to treat specific diseases and ailments. *Aphthous stomatitis*, which produces sores on the mouth, gums and tongue, was studied first. Medical researchers do not know what causes this disease and the people who suffer from it have been treated in a variety of ways, including with the use of local anesthetics, antimicrobial products and topical steroids.

Researchers were keen to find out if *Zataria multiflora* could help. The team contacted the university's faculty of dentistry and located an oral hygiene specialist who was interested in becoming involved in this effort. This specialist conducted a clinical study and, again, the oil and extract both passed with flying colors. Such was their success that the Tolid Daru Pharmaceutical Company decided to formulate and produce a mouthwash for use against *Aphthous stomatitis*.

Similar collaborations between a physician, who conducted the clinical study, and Tolid Daru's chemists, who formulated a commercial cough medicine, were used to establish and exploit the plant's expectorant and cough-suppressing properties.

The biggest challenge, however, was still to come: How to convince doctors and patients to use drugs based on traditional plants? For decades, if not centuries, conventional modern medical practitioners have turned their backs on herbal medicines, believing such "medicines" to be nothing more than fanciful folk cures whose efficacy has not, and cannot, be scientifically established. It has not been easy encouraging them to take up the new drugs and the battle is not over yet. However, as more useful herbal medicines are scrutinized at scientific institutes that doctors respect and are then commercially produced by pharmaceutical companies that they trust, the going will get easier for these and future discoveries.

The project was greatly helped by following a carefully designed strategy that the project team expects to use in future work. In addition, having now established ties with other institutions and individuals, future collaborations are likely to be easier to establish, operate and maintain.

To encourage the involvement of people from other research institutions, universities, government and pharmaceutical companies, a system of paying royalties to those working on medicinal plant research and development projects has been established. Such a strategy will not only create incentives for the researchers but also generate funds that can be invested in future research activities.

Future Plans

The project team is now investigating other medicinal plants in collaboration with its partners from the *Zataria multiflora* project.

To help physicians, particularly those who have been trained or who work in developed countries overcome their distrust of herbal medicines, stringent laboratory testing on animals is being carried out as a way of encouraging physicians to pursue clinical testing.

Collaboration with other centres of excellence in the developing world would lead to the development of more useful herbal medicines and help to establish these medicines as solid, reliable alternatives to synthetic drugs.

Implementing Institution

Faculty of Pharmacy

Tehran University of Medical Sciences

Tehran

Iran

Phone: +98 21 6461178

Fax. +98 21 6406757

eMail: shafiee@nrcgeb.ac.ir