

Traditional Herbal Medicines for Modern Times

# Harmal: The Genus *Peganum*



Ephraim Shmaya Lansky  
Shifra Lansky  
Helena Maaria Paavilainen  
with a Preface by Andrew Weil



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# Harmal

The Genus *Peganum*

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*For Peganum harmala and the science of healing.*

**E.S.L.**

*For my family.*

**S.L.**

*In memory of my grandmother Eimi Lempinen,  
always listening and always supporting.*

**H.M.P.**





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# Foreword

One might ask: from where came the idea to research *Peganum harmala*? The answer is that the idea found the researchers, as much as they found it. As children, one of them (ESL) treasured the little Golden Guides, concise, colorful packets of information and plenty of color with titles like *Mammals, Fishes, Birds, Reptiles and Amphibians* (the favorite), *Trees*, and *Rocks and Minerals*. It was nostalgic, then, to have also acquired at some point to the family home an additional Golden Guide, written by Professor Richard Schultes of Harvard, and titled simply *Hallucinogenic Plants*. *P. harmala* is depicted in that book with minimal text, apologizing that not much was known about this Old World hallucinogen, which seemed to no longer be in use. That guide joined the others in the series as valued possessions. ESL had earlier encountered harmala alkaloids in undergraduate Natural Products Chemistry at New College, Sarasota, Florida, with Prof. Rodger W. Griffin, who encouraged him to concentrate his interest in indolic chemistry for the sake of that seminar on the smaller indolics—lysergics would make the study unwieldy—it was to be restricted to simple substituted tryptamines and the harmala alkaloids, with harmala as the limit in chemical complexity. Only decades later while searching botanical candidates for putative complementary cancerology were harmala alkaloids encountered again, in what seemed a surprising context.

Some words of caution are in order. First, though *P. harmala* can be widely used safely in medicine, it *is* classified worldwide as a poisonous plant. Due to its monoamine oxidase inhibiting action, it will generally be contraindicated when SSRIs and other antidepressants or antipsychotic drugs are being used. It inhibits cytochrome P450 enzymes (Zhao et al. 2011), so when taken along with drugs dependent on P450 facilitated metabolism, e.g., statins, must be understood by the prescribing physician. One should be assiduously careful if taking other drugs at the same time, and always under strict and compassionate medical supervision.

However, the real and consistent danger underscoring all poisonings and fatalities from *P. harmala* described in the literature (Berdai et al. 2014; Mahmoudian et al. 2002; Moshiri et al. 2013) has been overdosing. A person either does not understand what harmal is (a poisonous plant with the potential to damage internal organs and kill), or otherwise, *does* know what harmal is and is overly enthusiastic to achieve some particular objective. There are fatalities reported every year from *P. harmala* poisoning worldwide. Please treat this plant with humility and respect. **NOTHING CONTAINED WITHIN THESE PAGES REPRESENTS ANY TYPE OF PRESCRIPTION, ENDORSEMENT, OR RECOMMENDATION FOR TREATING ANY AILMENT. IMPROPER USE OF *P. HARMALA* IN ANY FORM FOR PERSONAL USE CAN RESULT IN MORBIDITY AND DEATH. DO NOT TRY THIS AT HOME!**

In animals, harmal poisoning can be recognized by digestive and nervous syndromes—inebriation engenders a narcotic state interrupted by an occasional short period of excitement. Abortion is frequent in animals that digest this plant in a



dry year. In humans, vomiting and diarrhea can occur together with tremors, ataxia, bradycardia, delirium, hallucinations, and functional paralysis.

Nevertheless, the worldwide popularity of *P. harmala* is great. In a survey in a small Pakistani community, the inhabitants were queried about their use of 82 different medicinal plants. The leading preference among the 82 was for *P. harmala*, the second for *Punica granatum* (pomegranate), according to a preference scale as follows: *P. harmala* (0.93), *Punica granatum* (0.91), *Thymus mongolicus* (0.90), *Chenopodium album* (0.89), *Coriandrum sativum* (0.87), *Mentha longifolia* (0.87), *Lactuca serriola* (0.87), and *Portulaca oleracea* (0.87) (Aziz et al. 2016).

One aspect of this study was its globality—most feasible in the wired world. The contribution of scientists from Iran is singular, especially since Persia has been the seat of harmal and of the devotional culture that likely developed around it for thousands of years, and modern Iranian scientists continually report creative new uses for *P. harmala* in medicine and public health.

In China, trials and quiet experiments continue to methodically advance the medical use of harmal at all levels: *in vitro*, *in vivo*, and clinically. Much has been discovered through Chinese efforts in recent years regarding *Peganum*'s anticancer properties. *Harmalogy* thrives in China.

Scientific communities in many other countries also contribute, notably in Algeria, Egypt, Jordan, Morocco, Tunisia, Pakistan, India, Saudi Arabia, Iraq, Spain, Italy, and Turkey, where ancient knowledge of indigenous plants as medicines continues in daily life. More work, especially for synthetic harmala analogues, is done in Russia, Germany, France, Belgium, and England. As seen within, it is an *extremely* important and highly *utilitarian* herb for public health concerns (see use against pests, bacteria, fungi, and parasites in Chapter 7).

Persons seeking *P. harmala* for “recreational” hedonistic “light shows” and similar pleasures (Burillo-Putze et al. 2013) should be forewarned: (1) the blur between recreation and healing allows for considerable overlap, but if it is truly for recreational use, it should actually recreate—in a safe, physician-supervised, setting; (2) if the individual is looking for psychedelic shows, disappointment may occur. The psychoactive effect of harmal could easily be more subtle than expected, and physical discomforts including vomiting, headache, and difficulty in walking may occur. Overdose may cause a life-threatening emergency. **The possibility for unfavorable interactions with prescription drugs is real, very serious, and must always be considered. The physician prescribing for other drugs or supplements needs to ensure appropriate supervision prior to the use of harmal.**

Like the authors' previous works by CRC, *Figs: The Genus Ficus*, and *Caper: The Genus Capparis*, the pages to follow aspire to integrate ancient and indigenous ethnopharmacology with modern preclinical and clinical research, and as well to present something of the basis for the research through an exposition of its chemistry. The present work includes examples of direct clinical experience, self-inebriations, and subjective elaboration of the psychoactive effects of harmal and its extracts. Chapter 9 offers a speculative hypothesis of why psychoactive phytochemicals ranging from harmala alkaloids to cannabinoids exert anticancer effects clinically, based on a putative *retuning* of serotonin receptors on both neurons and lymphocytes.

In the Conclusion, the goal is to integrate the divergent streams of investigations and to reach elaborate possibilities for future research and collaborations.

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# Series Preface

Global warming and global travel are contributing factors in the spread of infectious diseases such as malaria, tuberculosis, hepatitis B, and HIV. These are not well controlled by the present drug regimes. Antibiotics are also failing because of bacterial resistance. Formerly less well-known tropical diseases are reaching new shores.

A whole range of illnesses, such as cancer, occur worldwide. Advances in molecular biology, including methods of *in vitro* testing for a required medical activity, give new opportunities to draw judiciously on the use and research of traditional herbal remedies from around the world. The reexamining of the herbal medicines must be done in a multidisciplinary manner.

There have been 51 volumes published since the start of the book series Medicinal and Aromatic Plants—Industrial Profiles in 1997. The series continues.

The same series editor, Dr. Roland Hardman, is also covering a second series entitled Traditional Herbal Medicines for Modern Times. Each volume of this series reports on the latest developments and discusses key topics relevant to interdisciplinary health sciences, research by ethnobiologists, taxonomists, conservationists, agronomists, chemists, pharmacologists, clinicians, and toxicologists. The series is relevant to all these scientists and will enable them to guide business, government agencies, and commerce in the complexities of these matters. The background to the subject is outlined next.

Over many centuries, the safety and limitations of herbal medicines have been established by their empirical use by the “healers” who also took a holistic approach. The healers are aware of the infrequent adverse effects and often know how to correct contraindications when they occur. Consequently, and ideally, the preclinical and clinical studies of an herbal medicine need to be carried out with the full cooperation of the traditional healer. The plant composition of the medicine, the stage of the development of the plant material, when it is to be collected from the wild or from its cultivation, its postharvest treatment, the preparation of the medicine, the dosage and frequency, and much other essential information is required. A consideration of the intellectual property rights and appropriate models of benefit sharing may also be necessary.

Wherever the medicine is being prepared, the first requirement is a well-documented reference collection of dried plant material. Such collections are encouraged by organizations including the World Health Organization and the United Nations Industrial Development Organization. The Royal Botanic Gardens at Kew (United Kingdom) is now increasing its collection of traditional Chinese dried plant material relevant to its purchase and use by those who sell or prescribe traditional Chinese medicine in the United Kingdom.

In any country, the control of the quality of plant raw material, of its efficacy, and of its safety in use is essential. The work requires sophisticated laboratory equipment and highly trained personnel. This kind of “control” cannot be applied to the locally produced herbal medicines in the rural areas of many countries, on which millions of people depend. Local traditional knowledge of the healers has to suffice.