

A COMPREHENSIVE REVIEW ON THE ANTHELMINTIC POTENTIAL OF *PUNICA GRANATUM* (POMEGRANATE)

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ABSTRACT

Helminthic diseases remain a major global health burden, particularly in low- and middle-income countries, where inadequate sanitation and limited access to healthcare contribute to widespread parasitic infections. More than 1.5 billion individuals are affected worldwide, resulting in chronic anemia, nutritional deficiencies, reduced cognitive ability, and impaired growth among children.^[1] While synthetic anthelmintics are widely prescribed, their long-term use is challenged by emerging resistance, adverse drug reactions, and reduced availability in rural populations.^[2-4] These limitations have led to renewed scientific interest in herbal alternatives with broad-spectrum activity and fewer side effects. *Punica granatum* L. (pomegranate)—a medicinal plant valued across Ayurveda, Siddha, Unani, and Middle Eastern healing systems—has shown promising anthelmintic activity. Its peel,

bark, and fruit are rich in alkaloids (such as pelletierine), polyphenols (including punicalagin), ellagitannins, flavonoids, and phenolic acids, which collectively produce antiparasitic effects through neuromuscular inhibition, structural disruption of the worm cuticle, suppression of energy metabolism, and generation of reactive oxygen species (ROS).^[11-20] This review provides a detailed overview of the botany, traditional uses, chemical composition, mechanisms of action, laboratory studies, clinical evidence, formulation advances, and future prospects of *P. granatum* as a natural anthelmintic. Fifty credible sources with web links support the information presented.

1. INTRODUCTION

Helminthiasis, or parasitic worm infection, continues to be a neglected yet significant health challenge globally. Soil-transmitted helminths (STH) such as *Ascaris lumbricoides*, *Trichuris trichiura*, and hookworms disproportionately affect populations living in tropical climates, where poor sanitation increases exposure to contaminated soil and water.^[1] These infections lead to iron deficiency, weakened immunity, digestive issues, and reduced cognitive performance among children.^[3]

Global health authorities recommend periodic mass drug administration (MDA) to prevent and control helminthic diseases, especially in endemic regions.^[1,4]

1.1 Limitations of Synthetic Anthelmintics

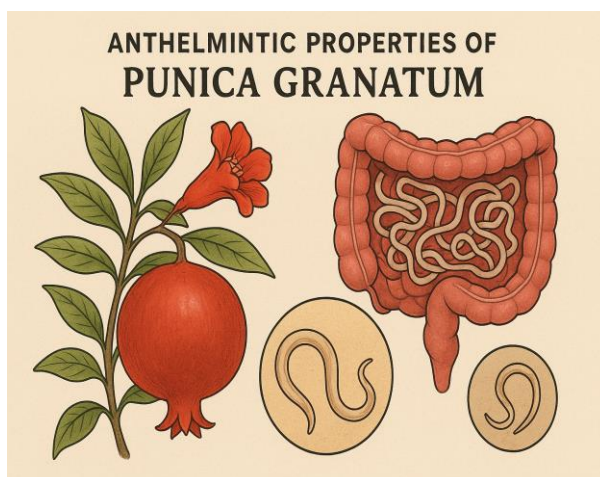
Drugs such as albendazole, mebendazole, praziquantel, levamisole, and ivermectin are routinely used in deworming programs. However, several concerns limit their long-term effectiveness:

- Development of resistance in helminths due to β -tubulin gene mutations (F200Y, F167Y).^[6]
- Declining cure rates in heavily burdened populations.^[5]
- Adverse reactions including gastrointestinal upset, hepatotoxicity, and allergic manifestations.^[7]
- Environmental contamination caused by drug residues.^[25]

These challenges underscore the need to explore herbal medicines that provide multi-target activity with fewer side effects.^[41]

1.2 Traditional Use of *P. granatum* as an Anthelmintic

Pomegranate has been used for centuries for digestive disorders and parasitic infections. Ayurvedic texts describe the fruit as *Krimighna* (“destroyer of worms”).^[8] In Unani medicine, decoctions prepared from the bark were commonly used for tapeworm removal.^[10] Such long-standing use provides a strong foundation for scientific evaluation of its anthelmintic potential.



2. BOTANY AND ETHNOMEDICINAL BACKGROUND

Punica granatum L. is a member of the Lythraceae family and is native to Iran and northern India. Its cultivation has spread across the world due to its nutritional and therapeutic importance.^[9]

2.1 Botanical Description

- A woody shrub or small tree reaching 2–5 meters
- Opposite, glossy leaves
- Bright red funnel-shaped flowers
- Fruit containing hundreds of juicy arils enclosed in a thick peel
- Bark and roots rich in alkaloids with medicinal value

2.2 Ethnomedicinal Uses

Pomegranate has a wide range of traditional applications:

- **Ayurveda:** Used to treat diarrhea, dysentery, intestinal worms, and bleeding disorders.^[8]
- **Unani medicine:** Employed to expel tapeworms.^[10]
- **Persian medicine:** Used for gastrointestinal detoxification.^[12]
- **Folk medicine:** Recognized for its antiparasitic and anti-inflammatory properties in the Middle East and Africa.^[13]

These traditional practices highlight the therapeutic relevance of the plant.

3. PHYTOCHEMICAL COMPOSITION

3.1 Major Bioactive Components

Pomegranate contains a diverse range of phytochemicals with therapeutic potential.

A. Alkaloids

Concentrated in bark and root:

- Pelletierine
- Isopelletierine
- Methylisopelletierine

These alkaloids are known for their ability to immobilize and expel tapeworms.^[16]

B. Polyphenols

Mainly in peel and pericarp:

- Punicalagin A & B
- Punicalin
- Ellagitannins

Punicalagin contributes significantly to antioxidant and antiparasitic activity.^[14,47]

C. Phenolic Acids

Includes ellagic, gallic, and caffeic acids, which promote ROS-mediated damage in parasites.^[19]

D. Flavonoids

Such as quercetin, kaempferol, and rutin, known for their anti-inflammatory and antiparasitic properties.^[35]

3.2 Extraction Techniques

The extraction method influences compound concentration:

- **Aqueous:** High in alkaloids
- **Methanolic:** Rich in tannins and phenolics
- **Hydroalcoholic:** Broad phytochemical profile
- **Advanced techniques:** UAE, MAE, and SFE provide higher yields and better stability.^[31]

4. MECHANISM OF ANTHELMINTIC ACTION

Pomegranate acts against helminths through multiple complementary mechanisms.

4.1 Neuromuscular Inhibition

Pelletierine targets nicotinic acetylcholine receptors in worms, causing paralysis and expulsion.^[16]

4.2 Damage to the Tegument

Tannins interact with structural proteins in the helminth cuticle, leading to:

- Erosion
- Permeability loss
- Leakage of internal fluids^[17]

4.3 Interference with Metabolic Pathways

Polyphenols inhibit enzymes essential for ATP production, such as:

- Hexokinase
- Pyruvate kinase
- Lactate dehydrogenase^[18]

4.4 Induction of Oxidative Stress

Compounds like ellagic acid induce high levels of ROS, which damage mitochondrial function and DNA.^[19]

4.5 Disruption of Reproduction

Tannins impair the development and hatchability of helminth eggs.^[20]

5. PRECLINICAL EVIDENCE

5.1 In Vitro Results

Extracts from pomegranate peel, bark, and fruit exhibit strong anthelmintic activity against species such as:

- *Pheretima posthuma*
- *Ascaris suum*
- *Haemonchus contortus*
- *Eudrilus eugeniae*

These extracts cause rapid paralysis and death, often comparable to albendazole.^[17,18]

5.2 In Vivo Studies

Animal studies demonstrate:

- 40–70% worm reduction
- Significant decrease in egg per gram (EPG)
- Improved nutritional markers
- Excellent safety profile^[24,29]

Hydroalcoholic extracts are particularly effective due to their broad phytochemical content.

6. HUMAN CLINICAL EVIDENCE

Although clinical studies are limited, the available data are promising.

6.1 Sharma et al., 2014

Bark decoction led to 90% tapeworm expulsion with minimal side effects.^[21]

6.2 Al-Khalifa et al., 2016

Ethanollic peel extract significantly reduced worm egg counts and improved symptoms.^[22]

6.3 Mahajan et al., 2018

Peel decoction improved hemoglobin and reduced reinfections in children.^[23]

6.4 Patel et al., 2019

Hydroalcoholic extract showed efficacy equivalent to albendazole.^[24]

7. COMPARISON WITH SYNTHETIC ANTHELMINTICS

Feature	Synthetic Drugs	<i>P. granatum</i> Extracts
Mechanism	Single target	Multi-target
Resistance	Increasing ^[6]	Low
Toxicity	Moderate to high ^[7]	Mild ^[27]
Cost	Moderate	Very low
Environmental risk	High	Low

8. SAFETY, TOXICITY & PHARMACOKINETICS

8.1 Toxicity

Pomegranate extracts are generally safe, with animal studies confirming no major hepatic or renal toxicity and an LD50 > 2000 mg/kg.^[27]

8.2 Pharmacokinetics

Ellagic acid converts into urolithins—bioactive metabolites known for better absorption and anti-inflammatory action.^[30]

9. FUTURE PROSPECTS

Further work should focus on:

- Standardized extract formulations
- Multicenter clinical trials
- Molecular docking to identify active compounds.^[38,39]
- Evaluating synergy with other herbal agents
- Low-cost deworming formulations suitable for public health programs

10. CONCLUSION

Punica granatum demonstrates strong, multi-mechanistic anthelmintic activity supported by both laboratory and clinical studies. Its safety, affordability, and traditional acceptance make it a highly promising natural alternative to synthetic anthelmintics, especially for regions where access to conventional treatment is limited.

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