

Exploring anticancer leads from bioactive compounds of Rutaceae family

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Abstract: In recent years, phytochemicals have attracted attention for their possible role in cancer treatment. Studies have shown that they can slow down the growth of cancer cells, trigger cell death and help control harmful processes in the body. However, most of this research is still at an early stage, mainly based on laboratory studies and more work is needed to confirm their safety and effectiveness in humans. But through traditional systems, medicinal plants continues to stay integrated with the well being of our lives and the family Rutaceae holds a special place among them. This family includes well-known plants such as *Aegle marmelos*, *Citrus* species, *Murraya koenigii*, *Ruta* and *Zanthoxylum*, many of which are commonly used in everyday remedies. These plants are rich in natural compounds like alkaloids, coumarins, flavonoids and essential oils, which are known for various health benefits. At the same time, with cancer cases increasing worldwide, there is a growing need to explore safer and more affordable treatment options. In this context, Rutaceae plants offer promising possibilities. This review focuses on their traditional uses, important chemical compounds and their potential role in cancer research, while also highlighting the need for further detailed studies.

Keywords: Cancer research, coumarins, novel leads, phytoconstituents, Rutaceae, traditional medicine

Introduction

The growing global cancer burden: according to World Health Organization and the International Agency for Research on Cancer (IARC), there were about 20 million new cancer cases and 9.7 million cancer deaths worldwide in 2022 and the number of new cases is projected to rise to more than 35 million by 2050, representing a 77% increase (WHO, 2024). While cancer is a rise is linked to population growth and ageing, as well as continued exposure to risk factors such as tobacco, alcohol, obesity, infections and air pollution (Anand et al., 2008). Medicinal plants in that context play an important role in global healthcare, not only in traditional systems but also as sources of modern therapeutic leads in areas of rising health crisis like cancer (Desai et al., 2008). The family Rutaceae is especially significant because it includes several medicinally valuable genera such as *Aegle*, *Citrus*, *Murraya*, *Ruta* and *Zanthoxylum*, many of which are rich in bioactive compounds like alkaloids, coumarins, flavonoids, limonoids and essential oils (Das et al., 2024). These phytochemicals have been widely studied for antioxidant, anti-inflammatory, antimicrobial, antidiabetic and anticancer properties (Kiran et al., 2025).

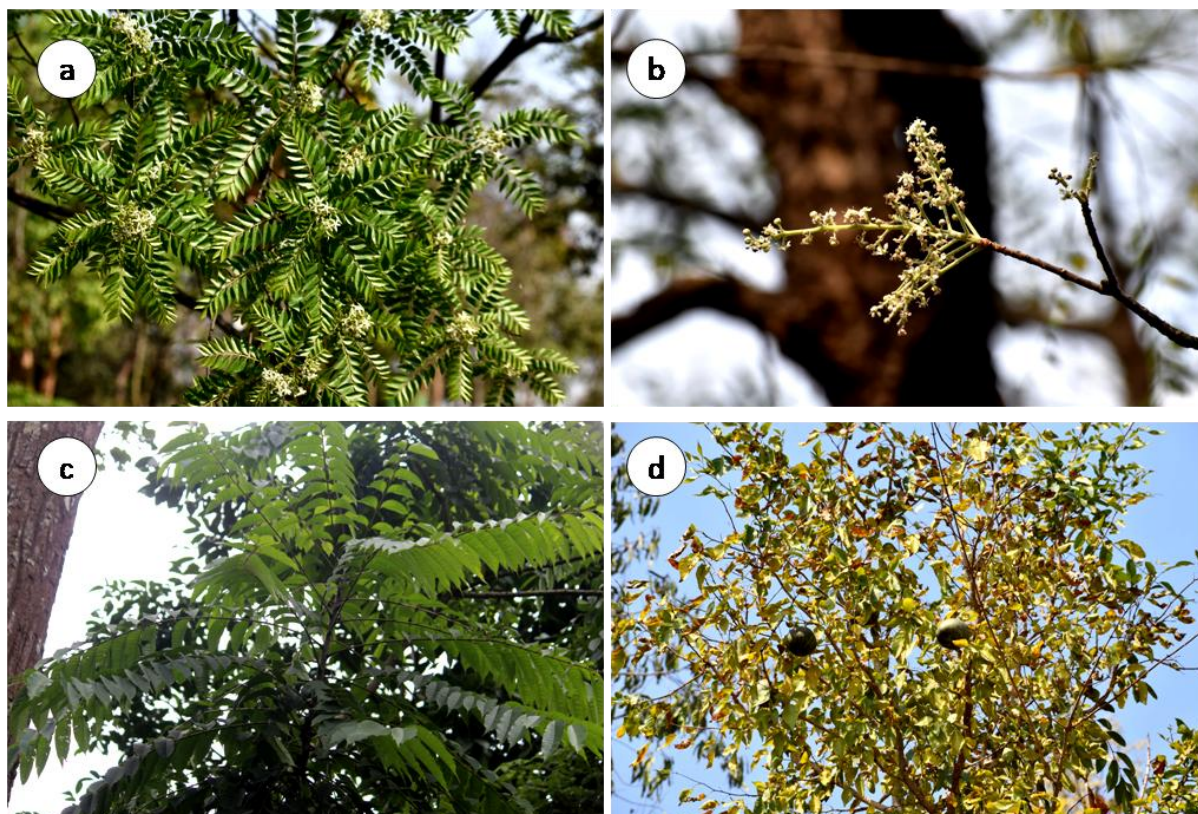


Plate 1: Members of Rutaceae family a) *Bergera koenigii* L. b) *Chloroxylon swietenia* DC. c) *Zanthoxylum retusum* (Albuq.) P.G.Waterman d) *Aegle marmelos* (L.) Corrêa

Among the diverse medicinal flora of Rutaceae (Plate 1), mostly trees or shrubs are found, though some are climbers and a few are herbs. They commonly possess pellucid glands filled with essential oils which is one their primary characteristics. Leaves are opposite or alternate, usually compound and lack stipules. The flowers are generally bisexual and regular, arranged in axillary or terminal

cymes or panicles and are rarely found in racemes. The fruit usually is a capsule, berry, drupe or may break into 1-4 capsular cocci. Seeds are usually one in each cell, sometimes many, with a variable seed coat and either fleshy or with no endosperm (Saxena and Brahmam, 1994). And, these morphological peculiarity of this family, adds on to their pharmacological diversity. This review has covered their medicinal uses in traditional and folk healthcare systems, important phytochemical classes, their reported and potential uses in cancer treatment and research.

Methodology

The present study is based on an extensive survey of published literature related to family Rutaceae. Scientific databases, including Google Scholar, Scopus, PubMed and Web of Science, were consulted to retrieve peer-reviewed research articles, review papers, ethnobotanical surveys and pharmacological studies. Keywords including “Rutaceae,” “medicinal uses,” “bioactive compounds,” “ethnopharmacology,” “cancer research”, “toxicity” and “phytochemistry” were used to identify relevant publications. Additionally, regional floras, theses, books and reports documenting traditional knowledge and distribution patterns were examined. Only studies containing verifiable scientific or ethnomedicinal data were considered. Information obtained was critically analyzed and systematically organized under thematic sections to ensure clarity and coherence (Kumar, 2025).

Ethnomedicinal uses

The literature study reveals that according to the 2026 dataset of Royal Botanic Garden, Kew, Rutaceae family has around 150 accepted genera and some 2100 species (Junior et al., 2023). Many members of the family are important in traditional healing systems that are used for digestive disorders, pain, inflammation, infections and metabolic conditions (Das et al., 2024; Kiran and Babu, 2025). Like, the fruit of *Aegle marmelos* is widely used for diarrhea and dysentery, while the peel of *Citrus reticulata* is used for digestive complaints. *Atalantia monophylla* leaves are applied externally for rheumatic pain and *Chloroxylon swietenia* leaf paste is used to treat fungal infections. The root decoction of *Clausena excavata* is taken for bowel disorders, whereas the leaf juice of *Glycosmis pentaphylla* is commonly used to manage eczema.

Phytoconstituents and anti-cancer properties

Members of the family Rutaceae are rich in secondary metabolites with promising anticancer properties. Among the most important are coumarins, furanocoumarins, alkaloids, limonoids and flavonoids, many of which have shown strong cytotoxic and antiproliferative effects *in vitro* and in some cases, *in vivo* (Narang and Jiraungkoorskul, 2016; Iqbal et al., 2017). Compounds such as auraptene, chalepentin, rutamarin, graveoline, skimmianine, limonin, tangeretin and carbazole alkaloids from *Murraya koenigii* have demonstrated activity against a wide range of cancer cell lines, including breast, colon, liver, gastric, pancreatic, leukemia, lymphoma and melanoma cells (Aniqa et al., 2022). Their effects are mediated through multiple mechanisms, including apoptosis induction, caspase activation, ROS generation and modulation of signaling pathways and apoptotic proteins.

And this proves that bioactive compounds from Rutaceae have potential for lead compounds in anticancer drug development (Table 1).

Table 1: Selected Rutaceae species with reported anticancer potential

Plant species	Important anticancer constituents	Reported activity	Source(s)
<i>Aegle marmelos</i> (L.) Corrêa	Lupeol, auraptene, skimmianine and other coumarins	Positive activity against lymphoma, leukemia, melanoma, breast cancer and liver cancer.	Junior et al., (2023)
<i>Citrus x aurantiifolia</i> (Christm.) Swingle	Limettin, isopimpinellin, limonexic acid and isolimonexic acid	Shows inhibitory effects against colon, pancreatic and breast cancer cells. Juice extract at 100 µg/ml reportedly inhibited 73-89% of Panc-28 pancreatic cancer cell growth after 96 hours with apoptosis linked to Bax, Bcl-2, caspase-3 and p53 expression.	Narang and Jiraungkoorskul, (2016); Iqbal et al., (2017)
<i>Citrus x limon</i> (L.) Osbeck	Methoxylated flavones	<i>In vitro</i> activity against human colon cancer.	Iqbal et al., (2017)
<i>Clausena lansium</i> (Lour.) Skeels	Clausenalansamid A and B	Reported activity against gastric and liver cancer cells.	
<i>Murraya koenigii</i> (L.) Spreng.	Carbazole alkaloids such as mahanine, mahanimbine and murrayanine	Potent anticancer activity against several cell lines.	

<i>Ruta chalepensis</i> L.	Chalepensin, rutamarin, graveoline / graveolin	Highly cytotoxic to leukemic and hepatic tumor cells; regarded as a promising source of antiproliferative compounds.	Iqbal et al., (2017); Elizondo-Luévano et al., (2023)
<i>Zanthoxylum</i> spp.	Acridone and furoquinoline alkaloids	Show cytotoxic and related bioactivities	Iqbal et al., (2017)

Research gaps

Although many species of the family Rutaceae have been reported to possess anticancer activity, the available evidence remains fragmented and uneven. Most of the studies are limited to *in vitro* cytotoxicity assays, while comparatively few have progressed to *in vivo*, preclinical or clinical evaluation. Important medicinal species such as *Aegle marmelos*, *Murraya koenigii*, *Ruta chalepensis*, *Citrus aurantifolia* and *Zanthoxylum* spp. have been explored to show promising bioactive compounds, yet the precise molecular mechanisms, pharmacokinetics, bioavailability, dose optimization and long-term safety of many of these metabolites are still insufficiently understood. There is also a lack of standardized extraction methods, chemoprofiling and reproducible bioassay-guided isolation, which makes comparison among the related studies difficult.

Future aspects

The future prospects of Rutaceae in anticancer research are highly promising. As, it contains a rich composition of coumarins, furanocoumarins, alkaloids, limonoids, flavonoids and terpenoids that may serve as lead molecules for the development of safer and more effective anticancer agents. Future studies may prioritize bioassay guided isolation, mechanistic studies and structure-activity relationship analysis to identify the most potent compounds and optimize their metabolic activity. *In vivo* validation, toxicological evaluation, formulation development and clinical translation may need greater emphasis.

Conclusion

The family Rutaceae occupies an important place among medicinal plants because of its wide ethnobotanical use and remarkable phytochemical diversity. Available studies indicate that Rutaceae-derived metabolites like coumarins and various alkaloids can inhibit cancer cell proliferation, induce apoptosis, modulate signaling pathways and suppress tumor progression, highlighting their value as potential therapeutic leads. A deeper understanding of their medicinal properties and active principles may support the development of novel, accessible and effective strategies for cancer prevention and treatment.

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