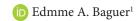
Mango (Mangifera indica L.) As a Model for Flavonoid **Studies**

El mango (Mangifera indica L.) como modelo de estudios de los flavonoides



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ABSTRACT

Currently, there is an increasing shift toward healthy eating, accompanied by the consumption of bioactive compounds that have been used as therapeutic agents in traditional medicine. The objective of this study is to compile part of the abundant information available on the use of mango (Mangifera indica L.), to understand its potential, and to analyze the direction of recent research related to the secondary metabolites of this fruit, which could be considered a model species due to its many benefits. A PRISMA methodology search was conducted, ensuring the use of uniform criteria across databases, including SCOPUS, SciELO, REDALYC, and Google Scholar as search engines. In recent years, extraction methods have improved, leading to advancements in applications and scientific studies that help explain its use in traditional medicine and project its future applications. However, it is important to emphasize that further research is needed, particularly due to the large groups of phytochemicals with highly specific actions, where low bioavailability must be considered in in vivo experiments and treatments.

Keywords: Mango (*Mangifera indica* L.), antioxidants, traditional medicine.

RESUMEN

En la actualidad, cada vez más se está recurriendo a la alimentación saludable y junto a ello, el consumo de los principios activos que han servido como terapéuticos en la conocida medicina tradicional. El objetivo del trabajo es aunar parte de la abundante información que existe sobre el uso del mango (Mangifera indica L.) para conocer su potencial, entender hacia donde se dirigen las investigaciones de los últimos años relacionadas con el uso de los metabolitos secundarios de este frutal, que bien podría considerarse un modelo por todas las bondades que brinda. Se ha realizado una búsqueda utilizando la metodología PRISMA para usar siempre los mismos criterios en las bases de datos SCOPUS, SciELO, REDALYC y Google Académico como motor de búsqueda. En los últimos años se han mejorado los métodos de extracción y con ello las aplicaciones y los estudios con un

carácter científico, que ayudan a explicar su uso en la medicina tradicional y a proyectar su futuro, aunque es importante recalcar que falta mucho por estudiar y dilucidar al estar frente a grupos de fitoquímicos muy grandes y de acciones muy específicas, donde la biodisponibilidad es baja y debe ser tenida en cuenta cuando se trate de experimentos y tratamientos in vivo.

Palabras clave: Mango (Mangifera indica L.) antioxidantes, medicina tradicional.

INTRODUCTION

According to reports and historical records, mango (Mangifera indica L.) originated more than 5,000 years ago in the Tamil Nadu and Kerala regions of southern India. From there, it began to spread through Portuguese traders, followed by English merchants, eventually reaching the West through Spanish explorers (Bompard, 1993; Mukherjee, 1985). Currently, mango production is a significant sector in several tropical and subtropical countries in Asia and Latin America, which together account for 87.18% of total exports. The leading producers include Mexico, Thailand, Brazil, Peru, India, and Pakistan, while major importers include the United States, the European Union, Saudi Arabia, and Canada (FAOSTAT, 2023).

The positioning of Peruvian mango production in the international market is due to favorable climatic conditions, varietal management, and growing global demand. At the national level, the Piura and Lambayeque provinces lead in production volume, while Cajamarca and Ancash stand out for their high yields (Carrasco, 2022). Among the cultivated varieties, Kent mango dominates, accounting for 82% of total production (Midagri, 2023).

In the current landscape, there is an increasing focus on food quality, mainly in relation to nutritional value, which in some cases surpasses the gastronomic value that has traditionally prevailed for

societies and the food industry. Fruits, regardless of geographical location, serve as a key reference in dietary discussions, as fresh fruit consumption is widely promoted, along with juices, desserts, and various processed dishes. Alongside this modern approach to nutrition, which is largely based on the consumption of fruits and vegetables, a scientific perspective is emerging that focuses on both nutritional and pharmacological aspects.

Over the years, the development of new technologies in chemical sciences has facilitated research into the pharmacological potential of plants, based on their traditional medicinal uses across different regions. It is known that traditional medicine remedies originate from macerated extracts of leaves, stems, flowers, and fruits, which have been used for generations to alleviate ailments and expand botanical knowledge. this accumulated Ultimately, transmitted knowledge has influenced the development of modern pharmaceuticals, which are derived from plant structures with demonstrated pharmacological activity.

Despite scientific advancements, traditional medicine remains an alternative option, even for preventive care, depending on socioeconomic and cultural factors. It is also chosen due to the known side effects of synthetic drugs. With the same raw materials, along with scientific knowledge of chemical structures with pharmacological

effects and the optimization of extraction and quantification methods, modernized traditional herbal medicine has become an increasingly utilized resource.

The effectiveness of plant-based treatments is likely due to the presence of phytochemicals, which are products of plant metabolism that play biological roles. Among these, antioxidants found in various plant structures have drawn significant interest. Some of these have been extensively studied, while others remain underexplored. However, they may explain many of the observed health benefits. Mango is no exception, and it could serve as a model species, given its widespread consumption as the most popular fruit worldwide (Jahurul et al., 2015). This high consumption rate has positive economic implications for both producers and consumers, reinforcing its presence in the food industry and gastronomy.

Additionally, mango has been traditionally used for the treatment of gastrointestinal, respiratory, genitourinary ailments; ophthalmological washes, also as an aphrodisiac, laxative and diuretic (Ediriweera et al., 2017 and Mirza et al., 2021). This is explained by the presence in the different parts of the plant of phytochemicals such as mangiferin, phenolic benzophenones, acids, antioxidants such as flavonoids, ascorbic acid, carotenoids, tocopherol (Kumar et al., 2021). The most abundant compounds in mango leaves that play an important role are phenolics, which include phenolic

acids, xanthones, benzophenones, tannins, terpenoids, and flavonoids.

More than 5,000 flavonoids have been identified (Martínez-Flores et al., 2002), classified into six major families based on their chemical structure. These are flavanones, flavanols, flavones, flavonols, anthocyanidins and isoflavonoids. These compounds are involved in various biological processes, flower such as pigmentation and fragrance, aiding pollinator attraction, in vivo elimination of reactive oxygen species (ROS), reducing oxidative stress, defense mechanisms against biotic and abiotic stress and plantmicroorganism interactions (Agati et al., 2020; Mierziak et al., 2014; Sivankalyani et al., 2016). Table 1 presents findings from Pereira et al. (2024), which detail studies on plant-based insecticides and their mechanisms of action.

Various publications report the ethnomedical uses of different parts of the mango plant in treating various pathologies, which has also led to new research proposals. In some cases, this has even resulted in the development of new pharmaceuticals, such as Vimang, which has demonstrated antioxidant, analgesic, and anti-inflammatory properties (Garrido *et al.*, 2004).

Numerous publications have discussed this topic in recent years. Table 2 presents some of the traditional medicinal uses of different parts of the mango plant for various ailments.

Table 1. Functions of flavonoids as crop insecticides

Function	Description	References
Feeding Disruptors	The deterrent effect on the feeding of most insect crop pests is frequently reported. It is suggested that insects die from starvation if they remain near treated leaves, especially in their larval stage. The proposed mechanism of action may involve the inhibition of digestive enzymes essential for digestion.	Stec <i>et al.</i> , 2019. Maazoun, et al., 2019.
Detoxification System Disruptors	Detoxifying enzymes transform toxic compounds into less toxic or non-toxic compounds that are normally excreted, protecting insects. In vivo studies have shown a reduction in carboxylesterase activity, which is related to insecticide resistance.	Camacho-Campos et al., 2020. Punia et al., 2022.
Growth, Development, and Reproduction Disruptors	Flavonoids affect the development and growth of insects, altering their life cycle by interfering with oviposition, hatching, molting (ecdysis), and fertility.	Puri <i>et al.</i> , 2022. Zhao <i>et al.</i> , 2021.

Table 2.Uses of different parts of the mango plant in traditional medicine

Plant Part	Phytochemical	Effects	References
Roots and Bark	Mangiferin.	Antioxidant, anti-inflammatory, antidiabetic, immunomodulatory, and antitumor. Bronchodilator: under study for asthma treatment.	Luo et al., 2012. Gbearssor et al., 2005. Loan et al., 2021.
Leaves	Mangiferin, phenolic acids, benzophenones, flavonoids, ascorbic acid, carotenoids, tocopherol, xanthones, tannins, terpenoids, and saponins	Antioxidant, antidiabetic, anti-inflammatory, antimicrobial (effective against gram-positive and gram-negative bacteria and yeasts), immunomodulatory, anti-obesity, anti-allergic, antifungal, antiparasitic, antipyretic, hepatoprotective, antidiarrheal, and antitumor. Antiviral: inhibits late-stage replication of HSV-2.	Amrita <i>et al.</i> , 2009. Kumar <i>et al.</i> , 2021. Mirza <i>et al.</i> , 2021.
Fruits	Mangiferin, isomangiferin, homomangiferin. polyphenols.	Hypoglycemic effect in diabetic rats. Anticancer effects in vitro against: Molt-4 leukemia, A549 lung cancer, MDA-MB-231 breast cancer, LnCap prostate cancer, SW-480 colon cancer, and non-cancerous CCD-18Co colon cell lines	Kim et al., 2012. Noratto et al., 2010.
Seeds	Gallic acid, pentagalloyl glucopyranose. Gallotannins.	Antimicrobial activity against Salmonella typhi, S. aureus, H. pylori. Anti-inflammatory, antimutagenic, anticancer. Associated with tyrosinase inhibition, a potent free radical scavenger, antioxidant, anti-inflammatory, and hepatoprotective properties.	Chanwitheesuk et al., 2007. Díaz-Gómez et al., 2013. Nithitanakool et al., 2009. Luo et al., 2014.

MATERIALS AND METHODS

The literature search was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology, based on the 2020 version. The search strategy was carried out using metasearch engines from the SCOPUS, SciELO, REDALYC databases, and Google Scholar as a search engine. The Boolean operator "AND" was used, and the search terms were Mango (Mangifera indica), traditional medicine, flavonoids, antioxidants, in both English and Spanish. Efforts were made to select recent publications, although in some cases, older sources were included due to the value of the information they provided.

RESULTS AND DISCUSSION

In the case of mango, laboratory research has been conducted based on findings from traditional medicine across different parts of the world, where it has been used as an aphrodisiac, analgesic, antineoplastic, anti-inflammatory, antipyretic, antisyphilitic, astringent, cardioprotective, carminative, and antidiarrheal. Additionally, it has been employed for the treatment of throat diseases, eruptions, constipation, pharyngopathy, hemoptysis, hemorrhages, bleeding hemorrhoids, wounds, hypodipsia, burns, anorexia, cough, ulcers, vomiting, urethral discharge, and vaginopathy, among other conditions (Bekoe et al., 2017; Garrido et al., 2004; Mansud, 2016; Tirado-Kulieva et al., 2021).

Experimental results suggesting the potential antineoplastic activity of various natural flavonoid compounds present in mango, combined with the growing interest in treatments for this type of disease, have led to studies that explore the relationship

between diet and cancer incidence. Some reports propose a possible link between fresh fruit and vegetable consumption and reduced risk of cancer. However, the specific compounds responsible and their concentrations remain unknown, leading to the understanding that such claims highlight the need for further research. The goal would be to determine whether supplementation with specific flavonoids could contribute to the prevention or treatment of the various diseases mentioned (Hernández *et al.*, 2021).

The widespread presence different flavonoid types has also resulted in inconsistent findings across studies. For example, catechins, beyond their antioxidant effect, have not been definitively linked to the prevention of specific diseases. Flavonoids such as apigenin, kaempferol, luteolin, myricetin, and quercetin have been studied more extensively due to their abundance in different plant structures. However, no positive effects have been found regarding the incidence or mortality rates associated with various types of cancer (Pérez, 2003).

Equally significant research efforts have been directed toward flavonoid bioavailability, which remains low due to limited absorption, extensive metabolism, and rapid excretion. In in vitro tests and animal experiments, the proposed effects of interest are observed only at higher concentrations than those typically achieved in human cells. This suggests that studies should be conducted at lower concentrations over a longer period, as well as investigating potential interactions with other molecules. In vitro, flavonoids exhibit antioxidant activity, which could positively impact overall health. However, these effects do not necessarily translate to

humans, where the high structural variability among flavonoid subclasses makes it difficult to generalize their absorption and bioavailability based solely on their structural classification. Other factors must also be considered, including interactions with other compounds, metabolism, absorption, and dietary differences across regions and seasons.

Studies have reported that, despite the high intake of flavonoids, their plasma and intracellular concentrations in humans are 100 to 1,000 times lower than those of other antioxidants such as ascorbate, uric acid, and glutathione (Day & Williamson, 2001; Gutiérrez-Grijalva *et al.*, 2016).

It is necessary to further investigate and incorporate into the "equation" of availability the effects of gastrointestinal processing on antioxidant activity. González et al. (2015) stated that even after cooking, most flavonoid glycosides remain intact in the small intestine. It is also important to consider interactions with the food matrix, as various authors agree that the presence of macronutrients influences the bioavailability of co-ingested flavonoids (Bordenave et al., 2014; González et al., 2015; Zhang et al., 2014). In vitro studies have demonstrated that milk proteins combined with flavonoids reduce their antioxidant capacity (Xiao et al., 2011). This was further confirmed in studies with healthy human volunteers, supporting previous findings (Lorenz *et al.*, 2007).

Additionally, it has been proposed that carbohydrate-rich foods may enhance flavonoid absorption by stimulating gastrointestinal motility.

CONCLUSION

As a perennial and dense tree, mango produces fruit year-round, adapts to different seasons through varietal management, and contains numerous phytochemicals in all its structures. Given its high consumption, it could be considered a model fruit for antioxidant research.

The large number of flavonoids and the limited knowledge about them make it insufficient to claim their role in the prevention or cure of specific pathologies, even though in vitro experiments generate reasonable doubt about their interference in the genesis of different diseases. Therefore, it is important to characterize the bioactive components of plant origin that make up the daily diet.

The bioaccessibility and bioavailability of phytochemicals in the human body are critical factors to consider when attempting to extrapolate the biological activity demonstrated in vitro, where significantly higher concentrations are used.

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