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Review Article

Review on Cassia Species of Wound Healing & Cytotoxic Activity

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ABSTRACT

The Cassia genus, belonging to the Fabaceae family, encompasses a variety of species traditionally employed in folk medicine. Various studies have highlighted their pharmacological efficacy, particularly in wound healing and anticancer applications. This review consolidates available scientific literature on the wound healing and cytotoxic potential of major Cassia species, their phytoconstituents, and mechanisms of action. Several anthraquinones have been isolated from the seeds of Cassia species. Sennosides, which are well known for their medicinal importance, have been detected in the leaves of the plant. Cassia species are already reported in the ancient ayurvedic literatures and literature survey indicated its use against various skin diseases such as ringworm, eczema, and scabies. Because of the high incidence of skin diseases, especially among the weaker section of the Indian population, it was felt worthwhile undertaking research on this plant. According to ayurveda the leaves and seeds are acrid, laxative, antiperiodic, anthelmintic, ophthalmic, liver tonic, cardiotonic and expectorant. The leaves and seeds are useful in leprosy, ringworm, flatulence, colic, dyspepsia, constipation, cough, bronchitis, cardiac disorders. Cassia species powder made from Cassia species seeds and Cassia species splits are some ancient natural ingredients.

INTRODUCTION

Medicinal plants have played an important role in health care and disease management for many years (Romero-daza, 2002). In recent years, the global demand for alternative medicine through primary health care has significantly increased.

According to Ayurveda, the leaves and seeds have hepatic, ophthalmic, anthelmintic, laxative, antiperiodic, and astringent properties, expectorant, cardiotonic, and tonic. Organic farms use of cassia species as a natural insecticide. Tephrosia seeds and other roasted seeds can be used in place of coffee. The pet food industry is the most common application for powdered cassia

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species. Wound is unavoidable throughout human life; about 6 million people suffer from chronic wounds that includes diabetes, ulcer and local infections. Chronic wounds may cause multiple organ failure or even lead to death Extracts from plants have demonstrated potentials in the treatment of wounds. Hence the need to evaluate the cytotoxicity, wound healing ability and chemical constituents of herbal plants is necessary. [1] Medicinal plants remain a rich source of bioactive compounds used in modern drug development. Among them, Cassia species have gained attention for their therapeutic versatility. Distributed in tropical and subtropical regions, species such as Cassia alata, Cassia fistula, Cassia tora, and Cassia occidentalis have been used in traditional remedies for skin ailments, infections, and tumors [2].

Phytochemistry of Cassia Species

The Cassia genus, part of the Fabaceae family, is rich in secondary metabolites that contribute to its wide range of pharmacological activities, particularly wound healing and cytotoxic effects. Numerous phytochemical studies have identified anthraquinones, flavonoids, tannins, glycosides, steroids, and phenolic compounds across various Cassia species.

1. Anthraquinones

Anthraquinones such as rhein, emodin, chrysophanol, and physcion are commonly found in Cassia species and are associated with cytotoxic and anti-inflammatory properties. For instance, emodin and chrysophanol isolated from Cassia tora and Cassia occidentalis have shown promising anticancer activities [3].

2. Flavonoids

Flavonoids including kaempferol, quercetin, and luteolin have been reported in Cassia alata and Cassia fistula. These compounds exhibit antioxidant, anti-inflammatory, and tissue-repairing properties that are beneficial in wound healing [4].

3. Phenolic Compounds

Phenolic acids such as gallic acid and ellagic acid have been identified in Cassia fistula bark and pods. These compounds contribute to free radical scavenging activity, which supports tissue regeneration [5].

4. Tannins and Glycosides

The bark and leaves of Cassia species contain high levels of tannins, which possess astringent properties and promote wound contraction. Cardiac and sennoside glycosides, primarily found in C. angustifolia and C. tora, also contribute to the biological activities [6].

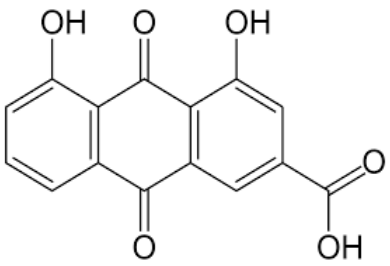
5. Essential Oils and Volatile Compounds

Essential oil analysis of Cassia alata and Cassia occidentalis reveals the presence of eugenol, linalool, and other volatile compounds that add to the antimicrobial and anti-inflammatory properties [7].

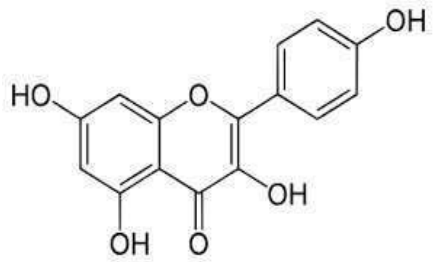
Representatives Phytochemical in key Species

Species	Major Compound Identified	Reported Activity
Cassia alata	Kaempferol, rhein, anthraquinone	Antioxidant, Anti-inflammatory
Cassia fistula	Gallic acid, Flavonoids	Wound healing, Antimicrobial
Cassia tora	Emodin, Chrysophanol, Sennosides	Cytotoxic, laxative, hepatoprotective
Cassia occidentalis	Aloe emodin, Physcion, Tanins	Anticancer, Antimicrobial

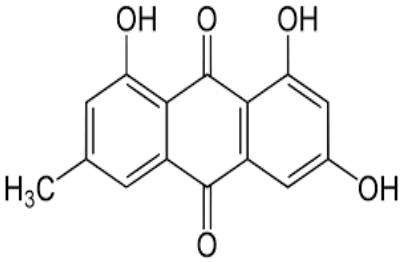
Chemical Structure of Phytochemicals



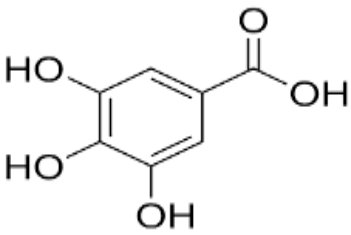
Rhein



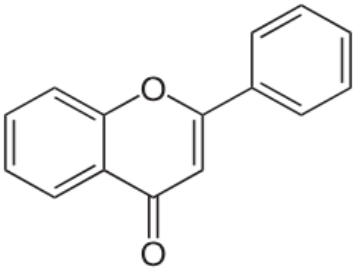
Kaempferol



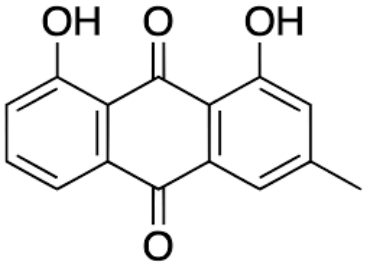
Emodin



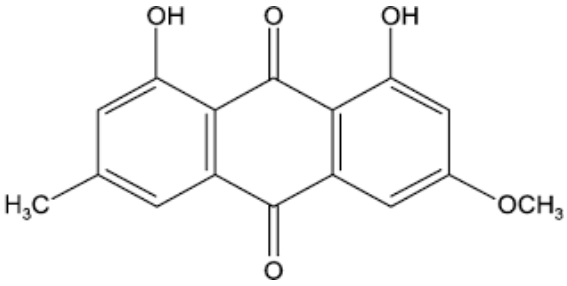
Gallic acid



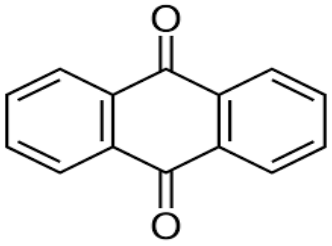
Flavonoid



Chrysophanol



Physcion

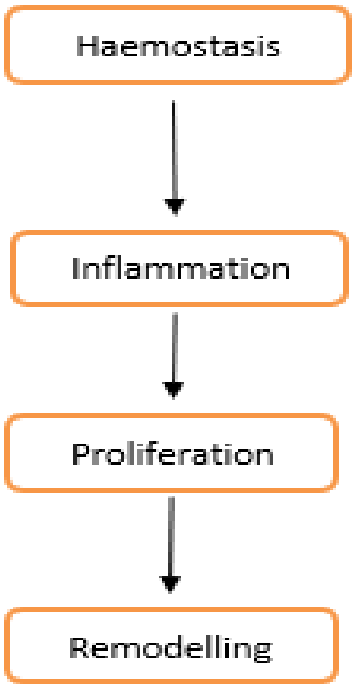


Anthraquinone

Wound Healing Mechanisms of *Cassia* Species

The wound healing process comprises four overlapping phases: hemostasis, inflammation, proliferation, and remodeling. *Cassia* species influence several of these stages through the following mechanisms:

Mechanism of Wound Healing:



1 Anti-inflammatory Effects

Cassia alata and *Cassia fistula* reduce inflammation by inhibiting pro-inflammatory cytokines such as TNF-α and IL-6 [8]. This promotes faster transition to the proliferation phase.

2 Antioxidant Activity

Flavonoids and phenolic acids scavenge reactive oxygen species (ROS), preventing oxidative stress-induced cell damage at the wound site [9].

3 Antimicrobial Activity

Species like *C. alata* exhibit antimicrobial action against *Staphylococcus aureus* and *Pseudomonas aeruginosa*, reducing the risk of wound infections [10].

4 Promotion of Collagen Synthesis

Extracts from *C. alata* and *C. occidentalis* enhance hydroxyproline content in wound tissues, which indicates improved collagen production and tissue repair [11].

5 Angiogenesis

Kaempferol and other flavonoids in *Cassia* upregulate VEGF expression, stimulating new blood vessel formation crucial for delivering nutrients to regenerating tissues [12].

Wound healing activity on cassia species

All dissection tools used in the assay were sterilized using 75% ethanol before use. The embryos were incubated for 11 days to allow good maturation of the chorioallantois membrane. On day 12 of incubation the outer shell was wiped with 75% ethanol to sterilize the surface. Under aseptic conditions a tiny hole was made carefully in the egg shell with a needle and a small window of the shell was cracked open exposing the opaque inner shell membrane. About 0.5-1 ml sterile saline was added to the inner shell membrane to make it translucent. This layer was then peeled to visualize the CAM layer. The CAM layer was

pulled gently by using sterile forceps and an excision wound of approximately 3 mm diameter was created in the CAM layer by using a small dissecting scissor. The drug saturated discs were then placed on the CAM of the embryos labeled with the corresponding concentrations and controls. The window on the egg shell was covered with para film and the eggs were returned to the incubator. Measurements of wound closure were made on alternative days up to day 5 of observation post wounding (25) The wound closure was measured as wound contraction percentage (WC %) by using the formula.

$$WC\ \% = \frac{\text{Initial wound size} - \text{Specific day wound size}}{\text{Initial wound size}} \times 100$$

Cytotoxic Activity

Cytotoxic activity refers to the capacity of a compound to cause damage to or induce the death of cells. It is a fundamental concept in oncology, pharmacology, and toxicology, often used to evaluate the potential of new drugs, particularly anticancer agents. Cytotoxicity studies help determine the therapeutic index of a compound, guiding further preclinical and clinical development (14)

Cassia species cytotoxic activity mechanism-

1. Apoptosis Induction:

a) Caspase Activation:

Many studies highlight the role of caspases, especially caspase 3 and 9, in Cassia-induced apoptosis. Cassia extracts have been shown to activate these caspases, which are key enzymes in the apoptotic cascade (15).

b) Mitochondrial Pathway:

Some research indicates that Cassia extracts can disrupt the mitochondrial pathway, leading to the release of cytochrome c, which further activates caspases and triggers apoptosis (16)

c) DNA Damage:

Certain Cassia compounds, like those found in Cassia alata and Cassia tora, can induce DNA damage, which can also initiate apoptosis (17)

2. Cell Proliferation Inhibition:

1) Concentration-Dependent Effects:

Studies show that Cassia extracts can inhibit the growth and proliferation of cancer cells in a dose-dependent manner (18)

2) Specific Cell Line Targeting:

Some Cassia species, like Cassia occidentalis, have been found to exhibit cytotoxicity towards specific cancer cell lines, suggesting that they may have targeted effects (19)

a) Anti-angiogenic Activity:

Some Cassia species, like Cassia tora, may inhibit the formation of new blood vessels, which are necessary for tumor growth, thereby limiting cell proliferation (20)

3) Metabolic Pathway Interference:

a) Glucose Uptake:

Some studies have shown that Cassia extracts can reduce glucose uptake in cancer cells. Glucose is a primary energy source for cancer cells, and its

reduction can disrupt their metabolism and growth (21)

b) Oxidative Stress:

Cassia extracts may induce oxidative stress in cancer cells, leading to cellular damage and apoptosis (22)

i) Inflammation Suppression:

Some Cassia species, like Cassia tora, can suppress inflammation by downregulating inflammatory genes like NF-κB, iNOS, and COX-2(23)

Cytotoxic Activity on Cassia Species

Brine shrimp lethality bioassay was used for probable cytotoxic action according to Persoon (1980). The eggs of Brine shrimp (Artemia salina Leach) were collected and hatched in a tank at a temperature around 37°C with constant oxygen supply. Two days were allowed to hatch and mature the nauplii. 4.0 mg of methanolic extracts of C. senna were taken and dissolved in 200µl of pure dimethyl sulfoxide (DMSO) to get stock solutions. By using the serial dilution method, a series of solutions of different concentrations were prepared from the stock solution and the concentrations were as; 100µg/ml, 50µg/ml, 25µg/ml, 12.5µg/ml, 6.25µg/ml, 3.125µg/ml, 1.5625µg/ml and 0.78125µg/ml, 0.3906µg/ml, 0.1953µg/ml. With the help of a Pasteur pipette 10 living nauplii were put to each of the vials. After 24 hours the vials were observed and the number of nauplii survived in each vial was counted. From this, the percentage of lethality of Brine Shrimp nauplii was calculated for each concentration of the extract. The effectiveness or the concentration-mortality relationship of plant product is usually expressed as a median lethal concentration (LC50) value (Meyer et al., 1982). This represents the concentration of the chemical that produces death in half of the test subjects after a certain exposure period. Vincristine sulphate with DMSO were used as a positive control group whereas DMSO was used as negative control group according to Tyler and Brady (1988); McKey (1994) and Lewis et al., (2005). If the brine shrimps in negative control group show a rapid mortality rate, then the test is considered as invalid as the nauplii died due to some reasons other than the cytotoxicity of the compounds (24)

LIMITATION

lack of clinical evidence based on in vitro in vivo models. Clinical trials confirms humans safety, efficacy and dosing. Different part of plant extract used then varying the result. Many extract made by using methanol, ethanol but they not safe for therapeutic use. High concentration extract rasing cytoxic and hemolytic activity, they cocern safety issue for open wound and sensitive skin.

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