A Comprehensive Review on some Species of *Mikania*

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ABSTRACT

Mikania is a genus of about 430 species belongs to family of Asteraceae. However, less than 10% of these species have been investigated. Amongst these, M. cordata, M. laevigata Schultz Bip. ex Baker and M. glomerata Spreng are considered medicinally important. Moreover, these herbs found their place for the treatment of flue, rheumatism and gastrointestinal disorders. The chemical studies have underlined the presence of various compounds; the main being terpenoids, flavonoids, volatile oil, carbohydrates and acids. Their extracts as well as pure isolated compounds, showed multiple pharmacological activities such as anti-inflammatory, respiratory tract diseases, antiulcer, antidiarrhoeal, antispasmodic, antimicrobial and others.

KEYWORDS: *Mikania, phytochemistry, pharmacological activities, toxicity studies*

INTRODUCTION

Mikania is a genus of about 430 species belongs to family of Asteraceae. The name honored to Czech botanist Johann Christian Mikan. However, less than 12% of 430 species of *Mikania* have been investigated [1,2]. Among them *M. cordata*, *M. laevigata* Schultz Bip. Ex Baker and *M. glomerata* Spreng are considered as medicinally important. These are mainly found in Brazil, Argentina, Paraguay, India, Uruguay, Sao Paulo and Rio Grande region. The members of this genus are mainly twinners and linans; climbs over shrubs and trees. There are many similarities occurs among them in the morphology, organoleptic characters and medicinal uses [3]. Although these three species found its place in Brazilian Pharmacopoeia and in some monographs [4,5], none have described the complete chemistry and pharmacology of these important medicinal plants. Therefore, we aimed to compile an up-to-

date and comprehensive review of *M. cordata, M. laevigata and M. glomerata* that covers its traditional and folk medicinal uses, phytochemistry, and pharmacology and toxicity study.

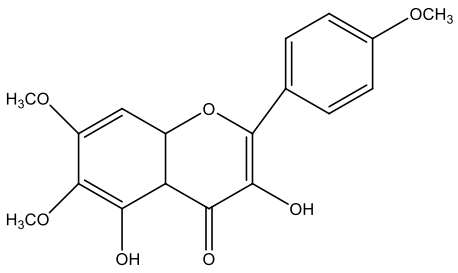
ETHNOMEDICINAL/TRADITIONAL USES

The *Mikania* species found its place for traditional uses mainly in Brazil. These *Mikania* species are commonly called as 'guaco' in Brazil. The guaco leaves has been traditionally used as extract, syrup or infusion to treat respiratory tract diseases like asthma, pleurisy bronchitis and cough. It also found its place for treatment of flue, rheumatism and gastrointestinal disorders [6,7,8].

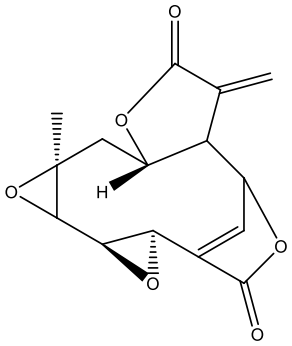
PHYTOCHEMISTRY

These plants generally reported to contain terpenoids, flavonoids, volatile oil, carbohydrates, and acids. *M. cordata* reported to contain mikanin, mikanolide, dihydromikanolide, deoxymikanolide, scandenolide, epifriedelinol, stigmasterol, friedelin, fumaric acid, α-pienene, β-pienene, α-thujene, germacrene D, glucose, fructose and other minor constituents [9,10,11]. In the case of *M. glomerata* the major constituents were coumarin, kaurenoic acid derivatives, lupeol, lupeol acetate, campesterol, β-sitosterol, spathulenol, caryophyllene oxide, sabinene, germacrene D along with some minor constituents [12,13]. Moreover, *M. laevigata* is rich in coumarin, germacrene D, spathulenol, myrcene, kaurenoic acid, grandifloric acid, syring aldehyde and others[14] (Fig. 1).

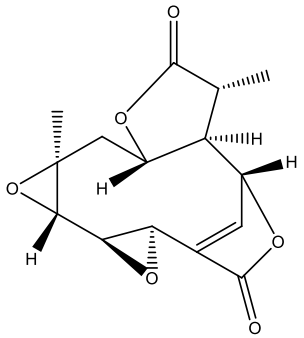
Figure 1. Structures of some chemical components of *Mikania*



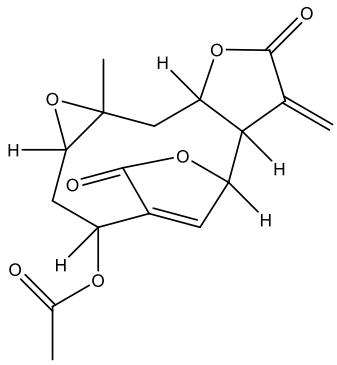
Mikanin



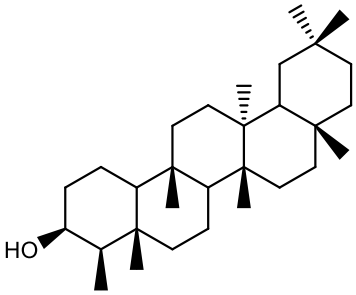
Mikanolide



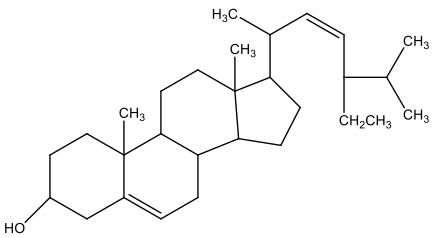
Dihydromikanolide



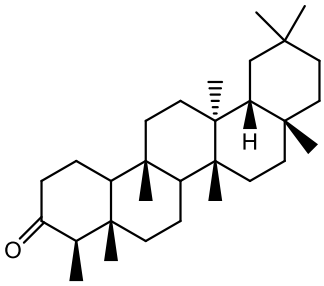
Scandenolide



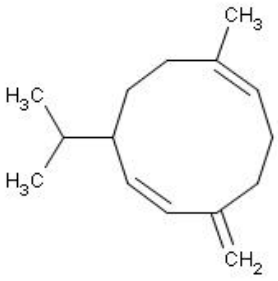
Epifriedelinol



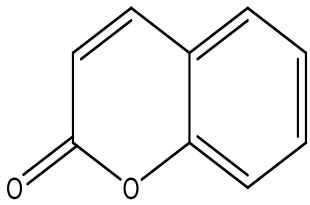
Stigmasterol



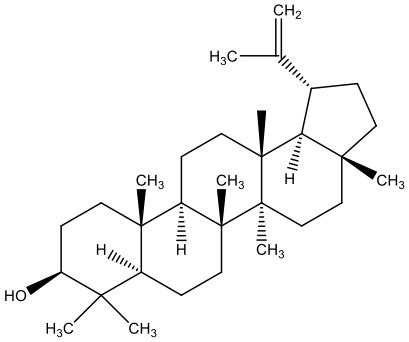
Friedelin



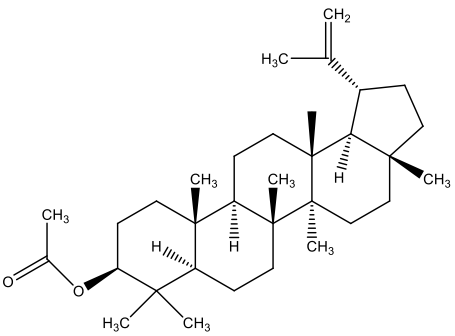
Germacrene D



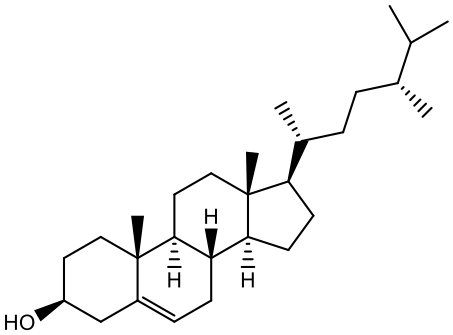
Coumarine



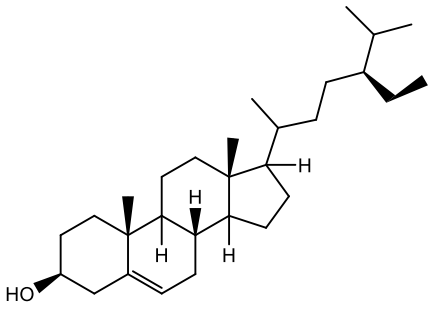
Lupeol



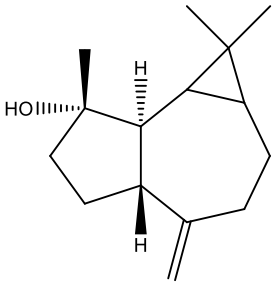
Lupeol acetate



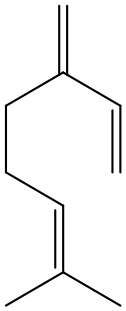
Campesterol



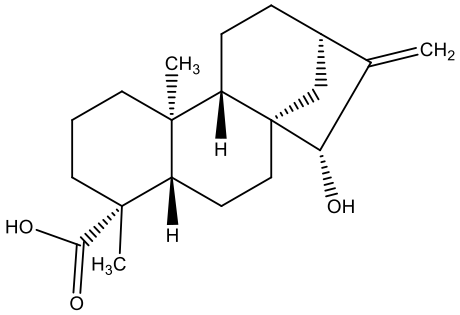
β-Sitosterol



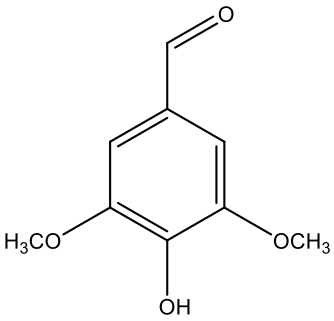
Spathulenol



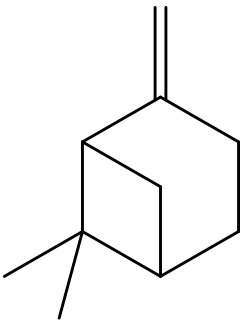
Myrcene



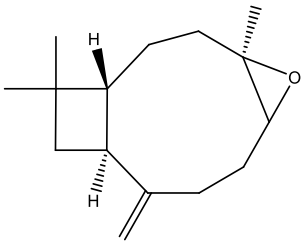
Grandifloric acid



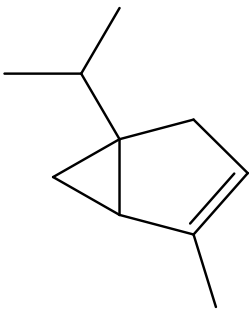
Syringaldehyde



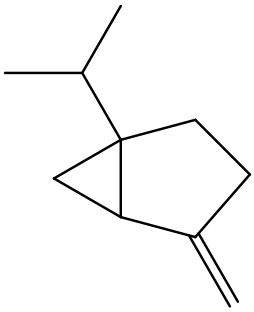
β-Pienene



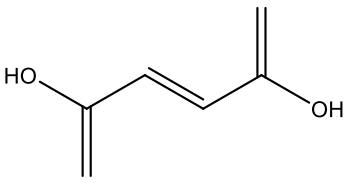
Caryophyllene



α-Thujene



Sabinene



Fumaric acid

PHARMACOLOGY

Several researchers have reported the different pharmacological activities of these three plants belonging to genus *Mikania in vitro* and *in vivo* models. Different parts of these plants have been found to exhibit several activities including anti-inflammatory, antiulcer, antidiarrhoeal, antispasmodic, and antimicrobial activities. These have been described in greater detail as follows.

Anti-inflammatory activity

The methanolic fraction of *M. glomerata* extract was found to inhibit carrageenin and mediator induced oedema especially due to inhibition of protein exudation, increased peritoneal capillary permeability and leucocyte migration in inflammatory condition. The extract also resulted the inhibition of sodium-furate induced experimental gout [15]. It found to be effective in inhibition of PAF-induced pleural neutrophil migration useful in immunogenic inflammation [16]. When *M. laevigata* decoction of leaves was investigated for anti-inflammatory activity in rat paw oedema and pleurisy models, it was found that the leaf decoction (200 mg/kg) inhibited oedema by 81.56% in rat paw oedema model while in pleurisy model the leaf decoction (400 mg/kg) inhibited leucocyte migration to pleural exudate by 28.26% [17].

Antiulcer activity

The methanolic fraction of *M. cordata* root extract was investigated for antiulcer activity in acetylsalicylic acid, serotonin and indomethacin induced ulcers in experimental rats and guinea pigs. It showed the significant protective action in gastric lesion in all these experimental models along with enhancement of acetic acid induced chronic gastric lesion [18]. The methanolic extract of *M. cordata roots* (50-150 mg/kg) prevented water immersion stress- (ED_{50}=95.1 mg/kg), ethanol- (ED_{50}=109.7 mg/kg), aspirin- (ED_{50}=125.5 mg/kg) and phenylbutazone-(ED_{50}=136.2 mg/kg) induced gastric ulcers and increased mucus secretion. These antiulcer activities might be due to modulation of defensive factors through an improvement of gastric cytoprotection [19].

When the alkaloidal fraction of *M. cordata* investigated for antiulcer activity against diclofenac sodium-induced gastrointestinal lesion in rats, it was found that the alkaloid rich extract (50 mg/kg) increased the stomach and duodenum pH, decreased ulcer index of stomach and duodenum without showing any symptoms of tissue damage. These results were found to be comparable or more potent than ranitidine hydrochloride [20,21]. Moreover, 70% hydroalcoholic extract of *M. laevigata* (1000 mg/kg) was found to decrease the ulcerative indomethacin-, ethanol-, stress- and reserpine-induced lesion index by 85%, 93%, 82% and 50% respectively. It was further noticed that the coumarin (100 mg/kg) and alcoholic extract (1000 mg/kg) decreased these lesions by inhibition of gastric acid secretion [22].

Antidiarrhoeal activity

M. glomerata has been used in Brazilian traditional medicine to treat gastrointestinal disorder. In order to determine its effect, in one experiment, the aqueous extract of leaves of *M. glomerata* assayed for the propulsive movements of the intestinal contents in mice. It

found to have significant antidiarrhoeal action, as that of loperamide, by inhibiting intestinal motility [23].

Antispasmodic activity

The ethanolic and hydro-ethanolic extracts of *M. glomerata* prepared by percolation and reflux; were investigated for antispasmodic activity on rat jejunum and guinea pig ileum elicted by acetyl choline (Ach) and histamine (Hist). These extracts were found as mixed antagonist. The ethanolic extracts obtained by percolation or reflux were more potent than hydro-ethanolic extracts (IC_{50}=0.082 and 0.103 mg/ml respectively for Hist and Ach). While, the hydro-ethanolic extracts obtained by percolation and reflux were found to have weakest activity (IC_{50}=0.324 and 3.594 mg/ml respectively for Hist and Ach). However, the main component coumarin was found to have no role in this activity [24].

Antimicrobial and antifungal activity

M. glomerata and *M. laevigata* extracts were investigated for antimicrobial activity.

Hydroalcoholic extract of *M. glomerata* showed antimicrobial activity against *S. faecium* (MIC=0.1 mg/ml); while *M. laevigata* showed the inhibition against *S. aureus* (MIC=0.04 mg/ml), *S. faecium* (MIC=0.35 mg/ml) and *B. subtilis* (MIC=0.09 mg/ml) [25]. In another study, the ethanolic, hexane and ethyl acetate fractions of *M. laevigata* and *M. glomerata* extracts were assayed for antimicrobial activity on growth and cell adherence of mutans streptococci. The hexane fraction of both plant extracts inhibited its growth (MIC=12.5-400 μg/ml and MBS=25-400 μg/ml) along with adherence of the microorganisms to a glass surface[26]. The ethanolic extract of *M. cordata* was found to show antifungal activity against phytopathogenic organisms *A. alternate, C. lunata, F. equiseti, M. phaseolina, B. theobromae* and *C. corchori* [27].

Effect on bronchi

M. glomerata and *M. laevigata* has been used in Brazilian folk medicine for the treatment of respiratory tract diseases. In order to decide its place, in one study, the ethanol: water (70:30) extract (100 mg/kg) of leaves of both these plants were investigated for its effect in pulmonary inflammation caused by acute coal dust exposure in rats. It was found that LDH activity and cell count decreased by *M. laevigata* extract, whereas *M. glomerata* extract only decreased the cell count increased during coal-dust exposure in rats. Both extracts also found to diminish lung inflammatory infiltration induced by coal dust while other parameters like myeloperoxidase and TBARS levels were found to be unchanged[28]. In another study, the hydroalcoholic extract of *M. laevigata* induces a concentration dependant relaxation of rat trachea which might be due to cellular mobilization of calcium perhaps due to a direct effect on membrane potassium channel. It was also found to be effective in allergic pneumonitis [29,30]. The aqueous and hydro-alcoholic extracts and dichloromethane fraction of *M. glomerata* leaves upon investigation for its effect on isolated respiratory and vascular smooth muscle; found that the hydro-alcoholic extract induced a concentration dependent relaxation on guinea pig trachea precontracted with histamine (IC_{50}=0.34 mg/ml), Ach (IC_{50}=0.72 mg/ml) or K^+ (IC_{50}=1.4 mg/ml) and on isolated human bronchi precontracted with K^+ (IC_{50}=0.017 mg/ml). It also showed a small vasodilatation on isolated mesenteric vascular

bed and on the isolated rat aorta along with significant relaxation of the oedema induced by *Bothrops jararaca* venoms in mice [31].

Analgesic and antipyretic activity

M. cordata crude extract and its methanolic extract were investigated for analgesic and antipyretic activity on rats. It showed that the crude extract (1-3 g/kg) and a sesquiterpene dilactone- deoxymikanolide (10 mg/kg) had a promising analgesic activity[9], while methanolic extract showed a significant antipyretic activity [15].

Antiallergic activity

The methanolic fraction of *M. glomerata* extract was evaluated for antiallergic action on oval albumin-induced allergic pleurisy. It was found to show significant decrease in plasma exudation as well as neutrophil and eosinophil infiltration [16].

Antistress activity

Methanolic extract of *M. cordata* roots upon evaluation for its antistress activity in albino mice; showed that at dose of 50-150 mg/kg, it increased the survival time of swimming in mice, improved swimming performance, prevented stress induced adrenal function changes, milk-induced leucocytosis, stress-induced gastric ulceration [32]. These effects were found due to the decreased in level of Ad, NA, DA and 5-HT along with marked inhibition of brain MAO and stimulation of SDH activities in brain and in liver [33].

Antimutagenic potential

Aqueous extract of *M. laevigata* on investigation for the presence of mutagenic activity in Salmonella/microsome assay; found that *M. laevigata* extract was negative for mutagenic potential but showed high percentage of inhibition of mutagenesis induced by mutagens 2AF in presence of exogenous metabolism (S9 fraction), for frame shift (TA98) and base pair substitution (TA100) lesion. Moreover it showed the inhibition against mutagens SAZ without exogenous metabolism. It also showed synergistic effect in frameshift mutation. However, these effects were found probably due to interaction of different active principles of the extract with genetic material [34].

Drug detoxifying potential

M. cordata proved a significant role in hepatic biotransformation system. Methanolic roots extract (50-150 mg/kg) was found to have no or little effect on microsomal cytochrome P-450, cytochrome b5 contents and NADPH cytochrome c reductase; It increased the level of microsomal uridine diphosphoglucuronyl transferase, microsomal uridine diphosphoglucose dehydrogenase while reduced the level of nicotinamide adenine dinucleotide (phosphate): quinine reductase and cytosolic glutathione S-transferase. These results showed the potential of *M. cordata* extract for the biotransformation of harmful chemical substances [35].

Liver tissue repairing activity

Researchers showed that *M. cordata* root extract may alleviate the deleterious effects of CCl_4, for that *M. cordata* root extract was tested for tissue repair activity in mice intoxicated with

CCl_4. It resulted that *M. cordata* root extract (150 mg/kg) dramatically improved the level of hepatic microsomal RNA (42.2%) and cytochrome P-450 content (70.2%) altered by CCl_4. The study demonstrates the activation of hepatic reticuloendothelial system–mediated defense mechanism as well as regeneration of protein synthesis [36].When the *M. cordata* extract was investigated for the study of its effect on the protein synthesis *in vivo* CCl_4 induced liver. It resulted the marked enhancement in the level of hepatic RNA, DNA and protein content at a dose of 100 mg/kg in mice, clearly indicated the tissue repair activity. It also influenced the lipid peroxidation process in liver tissue. It was found to inhibit the lipid peroxide level in liver homogenate (7.8%) at a dose of 10 mg/kg while it became (68.7%) at optimum dose of 150 mg/kg. It also decreased the level of enzymes- SGOT (15.6%), SGPT (13.4%) and LDH (22.8%) [37].

Effect on fatty acid profile

M. laevigata aqueous extract when investigated for fatty acid profile in lung and liver cells of Balb-C isogenic allergic pneumonitis bearing mice found that the level of arachidonic acid (ARA) and docosahexanoic acid (DHA) were distinct. In the liver, only DHA was altered while no significant differences in ARA production was observed. Further study showed that the aqueous extract, coumarines and *O*-coumarinic acid stimulated DHA synthesis ($P<0.05$) in the liver [14].

TOXICITY STUDY

Mikania species have been used in Brazil for many years for the treatment of various diseases. In order to determine its safety, in one study the “guaco” syrup was tested for its toxicity showed that the LD_{50} dose of guaco syrup was very high (10 g/kg) in rats; while upto 300 mg/kg it neither produce disturbances in haematological or biochemical parameters nor toxicity in hepatic, renal or pancreatic system [30]. In another study it was found to be safe in terms of reproductive system and on appearance of external organ [38].

SUMMARY AND CONCLUSION

In the present review, we have made an attempt to congregate the ethnomedicinal, phytochemical, pharmacological and toxicological information on *M. cordata*, *M. laevigata* and *M. glomerata*, medicinal herbs used in the Brazil, India and all over the world. Survey of literature revealed the presence of terpenoids, flavonoids, volatile oil, carbohydrates, acids and many other constituents. Preliminary report in experimental studies says it is significantly effective in diseases related to liver, lung and gastrointestinal tract. It is required to carryout pinpoint study related to such type of diseases. This review will definitely help the researchers as well as practitioners, dealing with these plants.

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