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Review Article
Momordica charantia Linn. (Cucurbitaceae): Review on Phytochemistry and Pharmacology

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Abstract
This review aims to present the information related to chemical composition of *Momordica charantia* Linn. (Cucurbitaceae), which is used in many Asian countries as a traditional functional food and medicine especially for the treatment of diabetes mellitus. Our main objective was to collect information about active constituents of this plant. Review of literature included PubMed searches with '*Momordica charantia*', 'Bitter gourd' or 'Bitter melon' as initial key words. The search was further refined by looking for terms such as 'Constituents' (or composition) and 'Activity' (or effect) within the results. The earliest report of the chemical screening of *M. charantia* dates back to 1960. Since then several classes of compounds including cucurbitacins, sterols, alkaloids, proteins and triterpenoids have been isolated. Cucurbitacins are reported to be the main active constituents of *M. charantia* that have anti-hyperglycemic, anti-hyperlipidemic, hepatoprotective, anti-obesity, anti-cancer and anti-viral activities. The *M. charantia* is a rich source of chemically novel compounds and needs elaborate screening strategies to dwell into the pharmacological effects of its phyto-constituents at the molecular level.

Key words: *Momordica charantia* L., bitter gourd, Cucurbitaceae, cucurbitacins, momordicosides

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

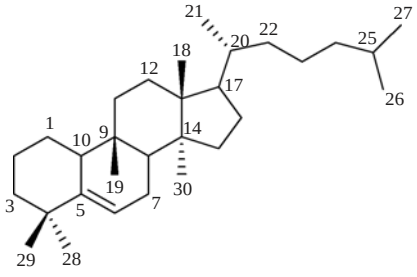
INTRODUCTION

Momordica is a genus of about 60 species of annual or perennial herbaceous climbers belonging to family Cucurbitaceae. *Momordica charantia* Linn. is a monoecious climber found in tropical and subtropical regions, often under cultivation up to an altitude of 1500 m. It is mainly found in Africa, Asia and Australia. Two varieties of *M. charantia* are cultivated in India *M. charantia* var., *charantia* with large fruits that are fusiform in shape and *M. charantia* var., *muricata* that are identified by small, round fruits[1]. *Momordica charantia* fruits are commonly consumed as vegetable, which has formed a part of subcontinental diet since centuries. Its fruits, seeds and leaves are traditionally used to treat diabetes mellitus across India[2]. The fruits are used as tonic, stomachic, stimulant, emetic, anti-bilious and laxative. Fruit-pulp, leaf juice and seeds are anthelmintic. Fruit is useful in gout, rheumatism and sub-acute spleen and liver malfunction. It is supposed to purify blood and dissipate melancholia and gross humors[3]. Leaf juice is given in bilious affections as emetic and purgative. Fruit and leaves are both administered internally in leprosy, piles and jaundice. Leaf-juice is rubbed to soles in the burning of feet. Leaf juice along with a little turmeric powder is given for the nausea of children, as it acts as emetic and thus cleanses the stomach. Externally it is applied to the scalp in pustular eruptions, to burns and boils[4].

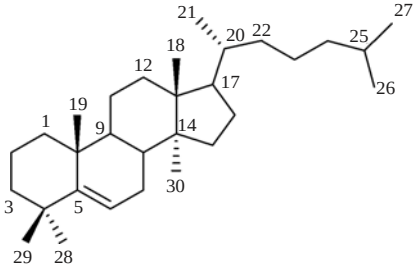
There are a few comprehensive reviews about the efficacy and safety and clinical of *M. charantia*[5,6]. However, despite exhaustive phytochemical screening, no review on the phytochemistry of this plant is available. Our main objective was to collect information about active constituents of this plant. Review of literature included PubMed searches with '*Momordica charantia*', 'Bitter gourd' or 'Bitter melon' as initial key words. The search was further refined by looking for terms such as 'Constituents' (or composition) and 'Activity' (or effect) within the results. This review summarizes previous and current information regarding its phytochemical and pharmacological screening.

PHYTOCHEMICAL REPORTS

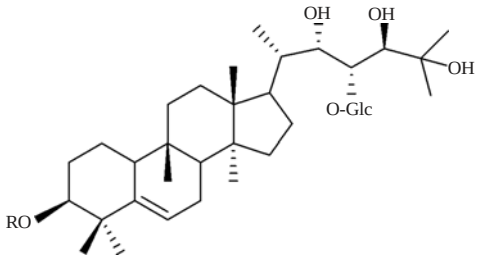
Momordica charantia mainly contains cucurbitacins[7-18], sterols[15,19,20], triterpenoids[16] and vicine[21]. The chemical structures of phyto-constituents isolated from *M. charantia* are summarized in Fig. 1.



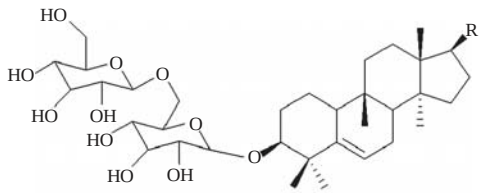
1 Cucurbit-5-ene



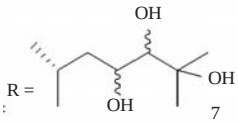
2 Lanost-5-ene



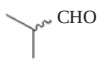
3 Momordicoside A R = Glc-(6→1)-Glc
4 Momordicoside B R = Xyl



5 Momordicoside C R =



7 Momordicoside E R =



6 Momordicoside D R =

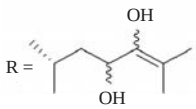
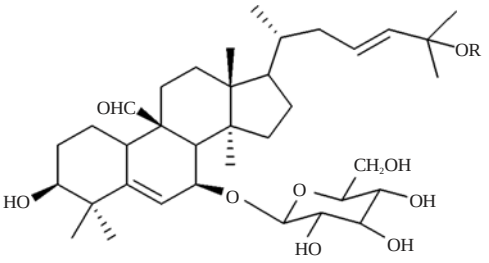
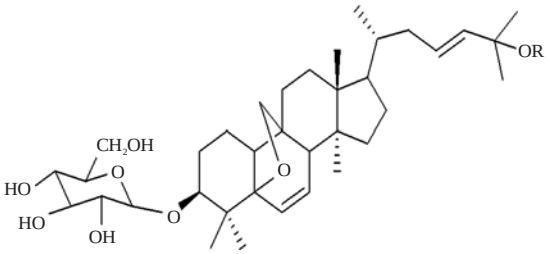


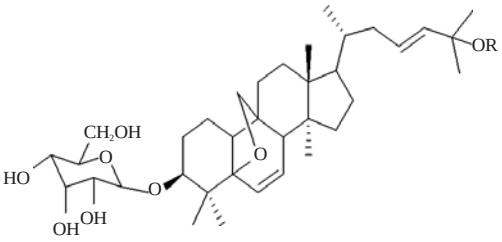
Fig. 1: Continue



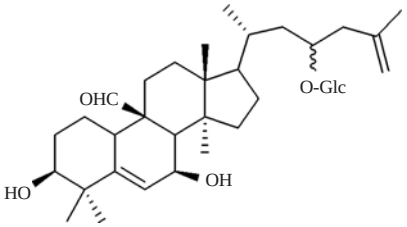
8 Momordicoside K R = CH_3



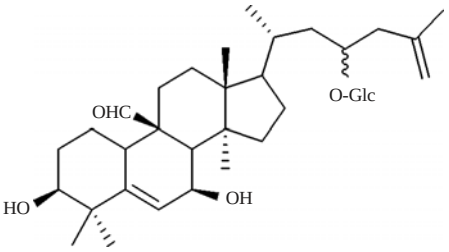
10 Momordicoside F1 R = CH_3
11 Momordicoside I R = H



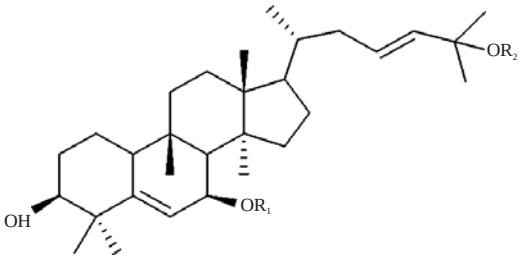
12 Momordicoside G R = CH_3
13 Momordicoside F2 R = H



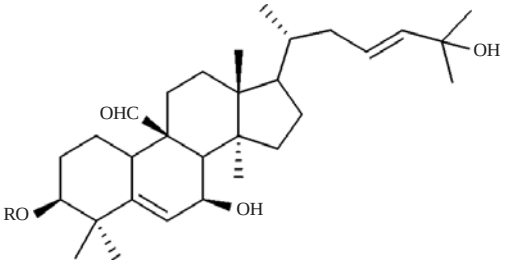
14 Momordicin I R = H
15 Momordicin II R = Glc



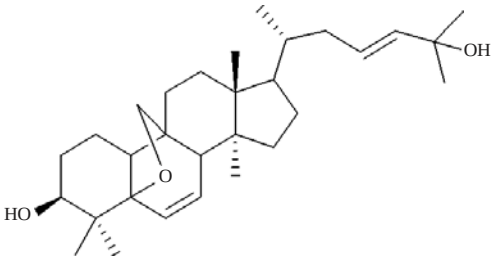
16 Momordicin III



17 3β,25-dihydroxy-7β-methoxy-cucurbita-5,23(E)-diene R_1 = Me, R_2 = H
18 3β-hydroxy-7β,25-dimethoxy-cucurbita-5,23(E)-diene $R_1 = R_2$ = Me

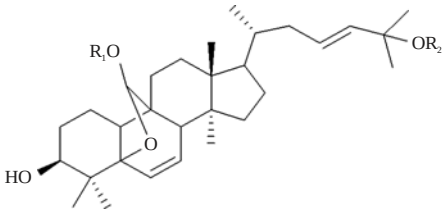


19 3-O-β-D-allopyranosyl 7β,25-dihydroxycucurbita-5,23(E)-dien-19-al R = All
20 3β,7β,25-trihydroxy-cucurbita-5,23(E)-dien-19-al R = H

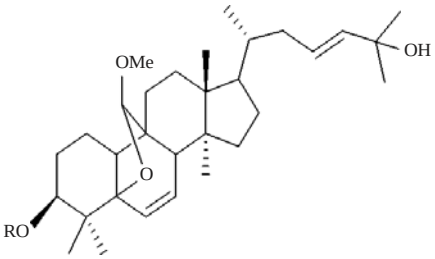


21 5β,19-epoxy-3β,25-dihydroxy-cucurbita-6,23(E)-diene

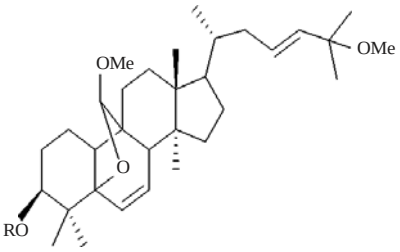
Fig. 1: Continue



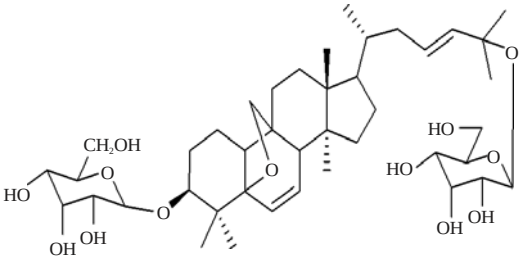
22 5β,19-epoxy-cucurbita-6,23(E)-diene-3β,19,25-triol $R_1 = R_2 = H$
23 5β,19-epoxy-19-methoxy-cucurbita-6,23(E)-diene-3β,25-diol $R_1 = Me, R_2 = H$
24 5β,19-epoxy-19,25-dimethoxy-cucurbita-6,23(E)-diene-3β-ol $R_1 = R_2 = Me$



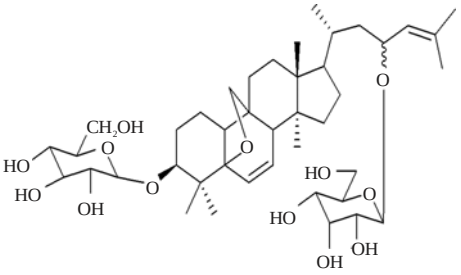
25 Goyaglycoside-a R = Glc
26 Goyaglycoside-b R = All



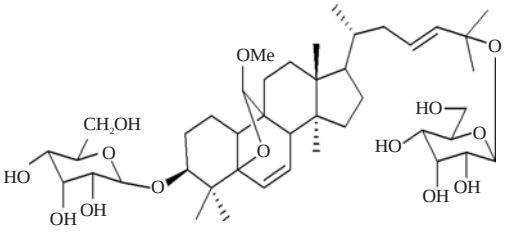
27 Goyaglycoside-c R = Glc
28 Goyaglycoside-d R = All



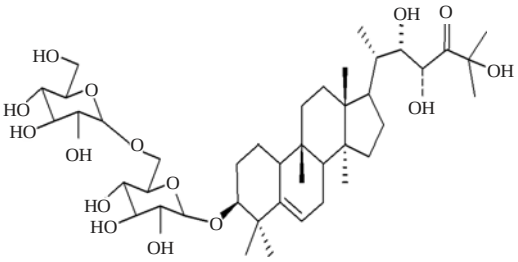
29 Goyaglycoside-e



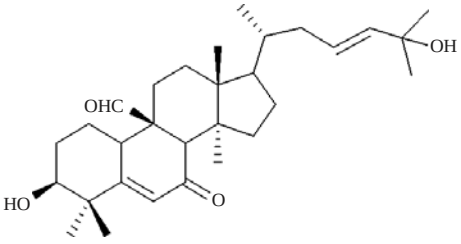
30 Goyaglycoside-f



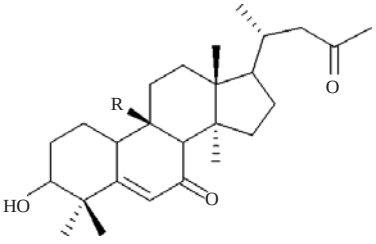
31 Goyaglycoside-g



32 Goyaglycoside-h

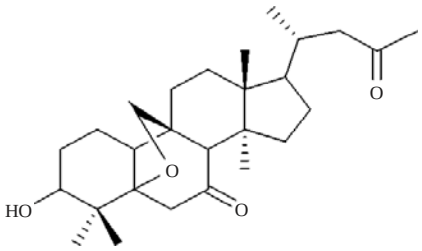


33 Kuguacin B

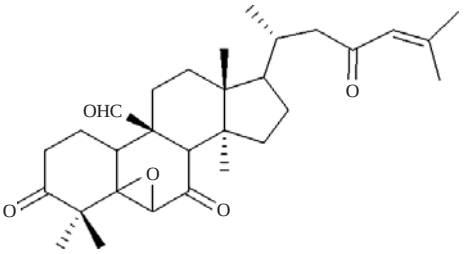


34 Kuguacin C R = CH_3
35 Kuguacin D R = CHO

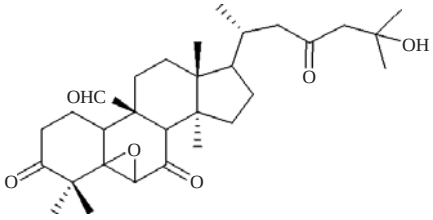
Fig. 1: Continue



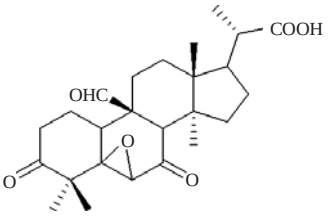
36 Kuguacin E



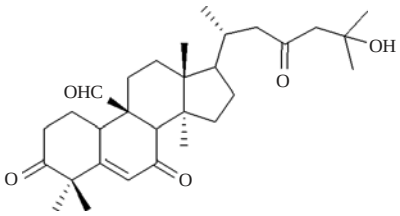
37 Kuguacin F



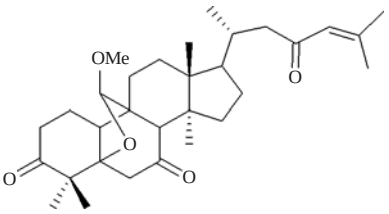
38 Kuguacin G



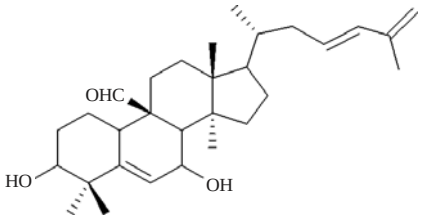
39 Kuguacin K



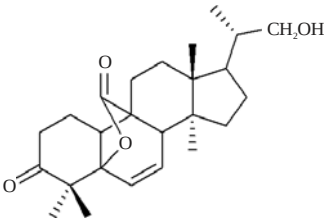
40 Kuguacin H



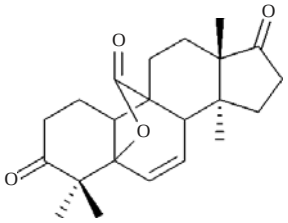
41 Kuguacin I



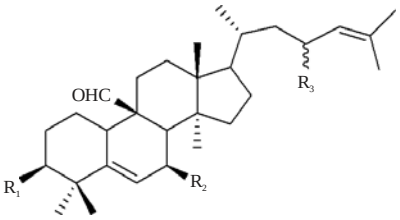
42 Kuguacin J



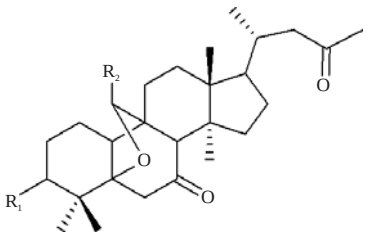
43 Kuguacin L



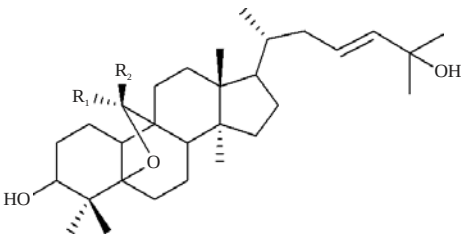
44 Kuguacin M



		R_1	R_2	R_3
45	Kuguacin N	OH	OH	=O
46	Kuguacin O	=O	=O	=O
46	Momordicin I	OH	OH	OH

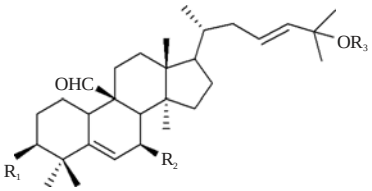


		R_1	R_2
47	Kuguacin P	=O	H
48	Kuguacin Q	=O	OCH_2CH_3

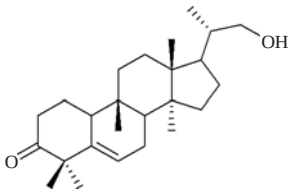


		R_1	R_2
49	Kuguacin R	OH	H
50	Karavilagenin D	=O	H

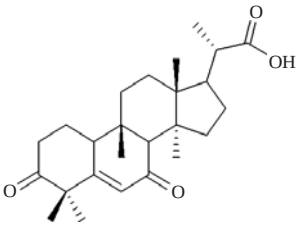
Fig. 1: Continue



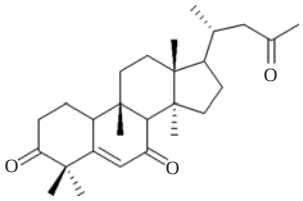
		R_1	R_2	R_3
51	Kuguacin S	=O	=O	H
52	3β,7β,25-trihydroxy-cucurbita-5,(23E)-dien-19-al	OH	OH	H
53	3β,7β-dihydroxy-25-methoxy-cucurbita-5,(23E)-dien-19-al	OH	OH	Me



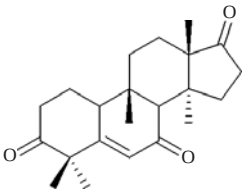
54 22-Hydroxy-3,24,25,26,27-pentanorcucurbit-5-en-3-one



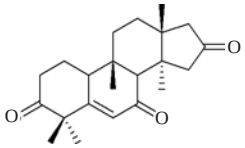
55 3,7-Dioxo-23,24,25,26,27-pentanorcucurbit-5-en-22-oic acid



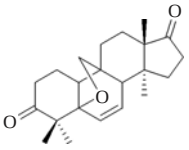
56 25,26,27-trinor-cucurbit-5-en-3,7,23-trione



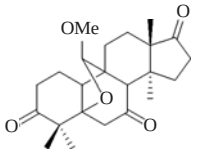
57 Octanorcucurbitacin A



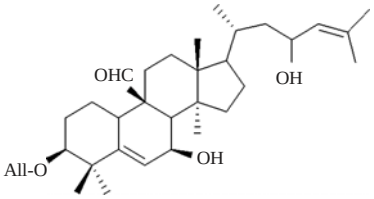
58 Octanorcucurbitacin B



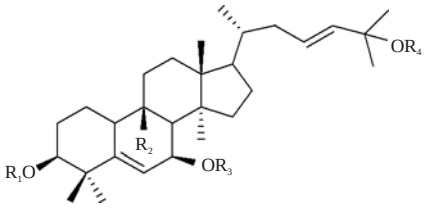
59 Octanorcucurbitacin C



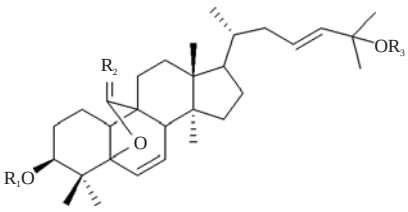
60 Octanorcucurbitacin D



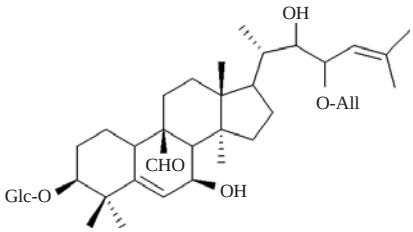
61 Charantoside B



		R_1	R_2	R_3	R_4
62	Charantoside A	All	CHO	Me	H
63	Karaviloside II	All	Me	Me	Me
64	Karaviloside III	All	Me	Me	H
65	7β,25-dihydroxy-cucurbita-5,23(E)-dien-19-al 3-O-β-D-allopyranosyl	All	CHO	H	H

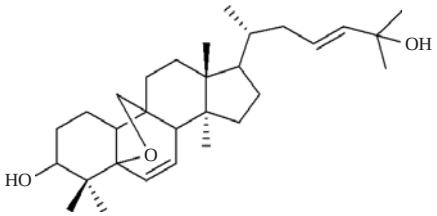


66 Charantoside C R = All, R_2 = O, R_3 = Me

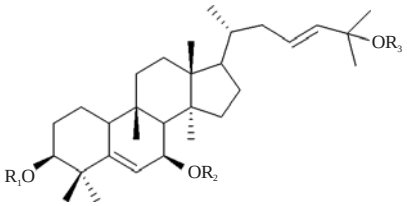


67 Momordicoside M

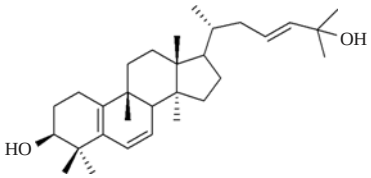
Fig. 1: Continue



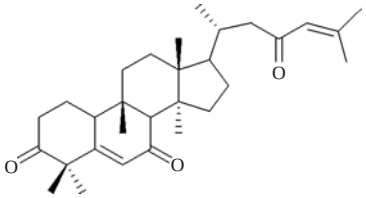
68 (23E)-5β,19-epoxy-cucurbita-6,23-diene-3β,25-diol



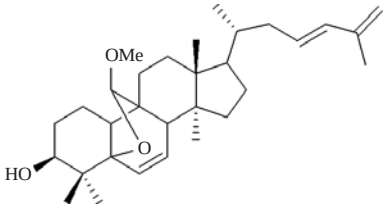
69 Cucurbita-5,23(E)-diene-3β,7β,25-triol R_1 = H, R_2 = H, R_3 = H
70 3β-Acetoxy-7β-methoxycucurbita-5, 23(E)-dien-25-ol R_1 = Ac, R_2 = Me, R_3 = H



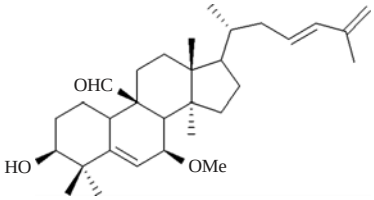
71 Cucurbita-5 (10),6,23 (E)-triene-3β,25-diol



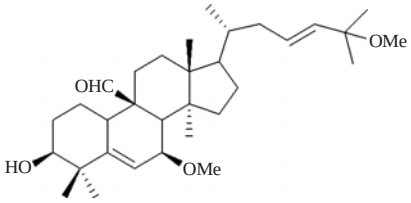
72 Cucurbita-5,24-diene-3,7,23-trione



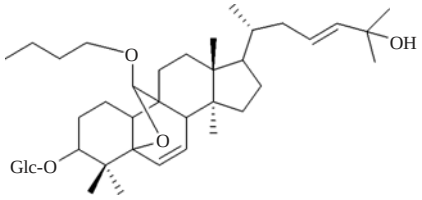
73 (19R, 23E)-5β,19-epoxy-19-methoxycucurbita-6,23,25-trien-3β-ol



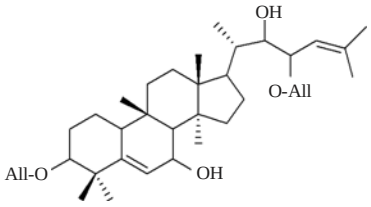
74 (23E)-3β-hydroxy-7β-methoxycucurbita-5,23,25-trien-19-al



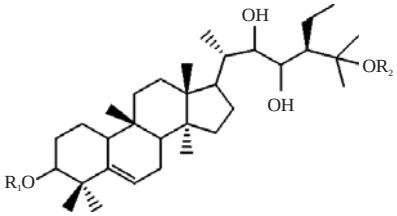
75 (23E)-3β-Hydroxy-7β,25-dimethoxycucurbita-5,23-dien-19-al



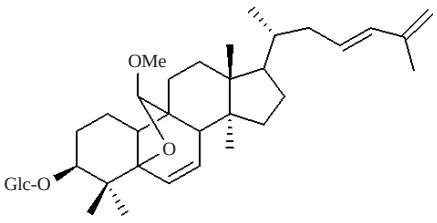
76 19(R)-n-butanoxy-5β,19-epoxycucurbita-6,23-diene-3β,25-diol 3-O-β-D-glucopyranoside



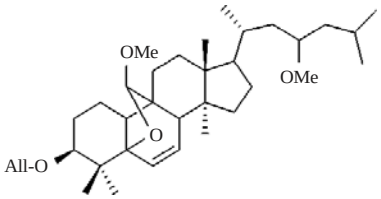
77 23-O-β-allopyranosylcucurbita-5,24-dien-7α, 3β,22(R),23(S)-tetraol-3-O-β-allopyranoside



78 23(R),24(S),25-trihydroxycucurbit-5-ene 3-O-{[β-glucopyranosyl(1→6)]-O-β-glucopyranosyl}-25-O-β-glucopyranoside R_1 = Glc-(6→1)-Glc; R_2 = Glc



79 Charantoside I



80 Charantoside II

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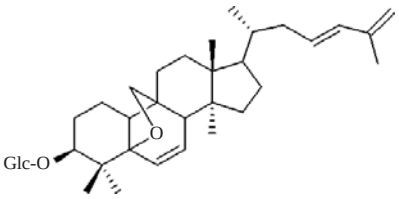
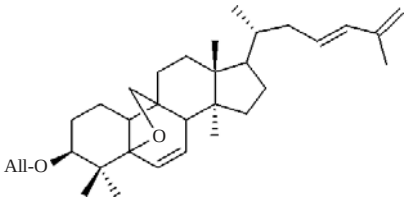
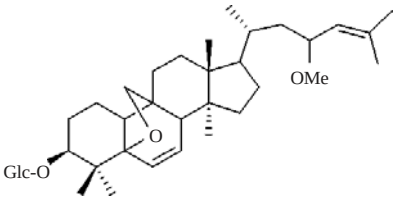


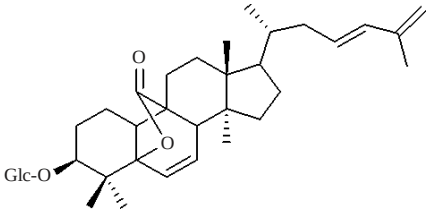
81 Charantoside III



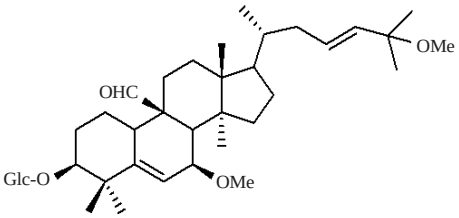
82 Charantoside IV



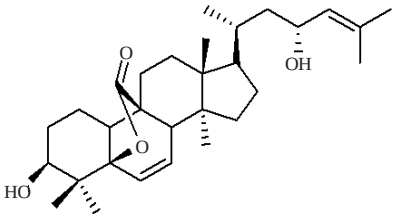
83 Charantoside V



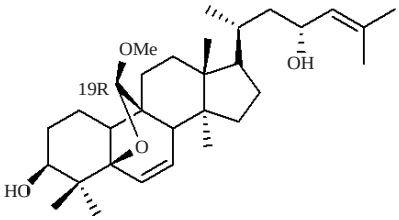
85 Charantoside VII



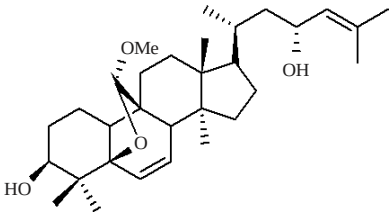
86 Charantoside VIII



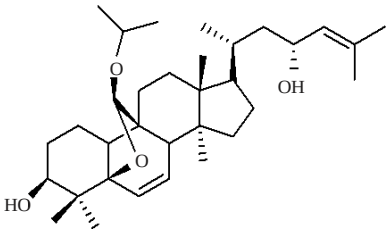
87 Cucurbita-6,24-dien-3β,23-diol-19,5β-olide



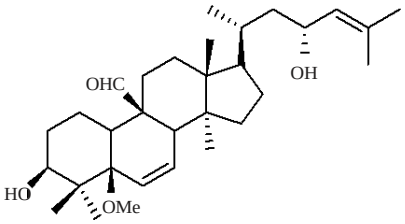
88 (19R)-5β,19-epoxy-19-methoxycucurbita-6,24-dien-3β,23-diol



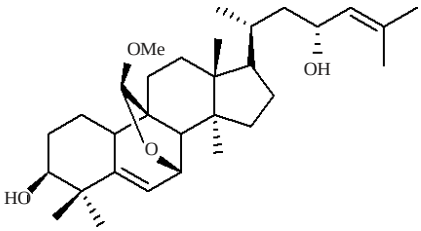
89 (19S)-5β,19-epoxy-19-methoxy-cucurbita-6,24-dien-3β,23-diol



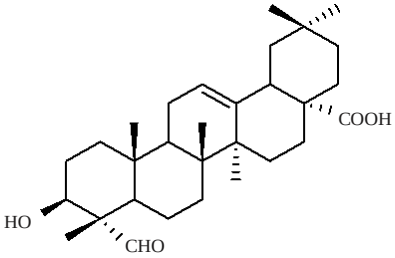
90 (19R)-5β,19-epoxy-19-isopropoxycucurbita-6,24-dien-3β,23-diol



91 3β,23-dihydroxy-5-methoxy-cucurbita-6,24-dien-19-al

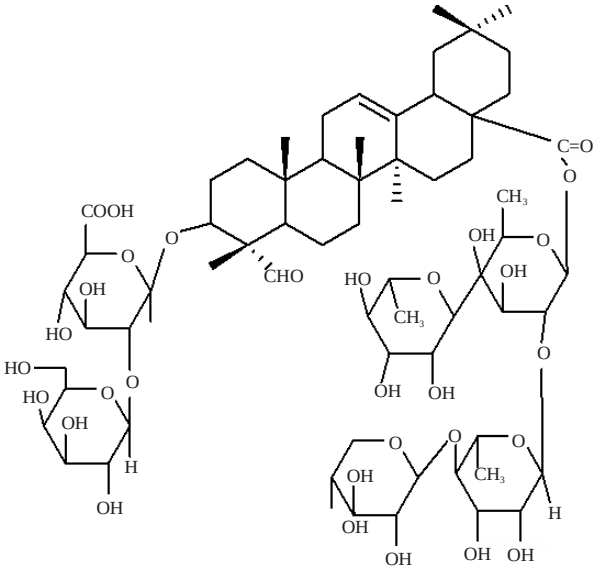


92 (19R)-7β,19-epoxy-19-methoxy-cucurbita-5,24-dien-3β, 23-dio

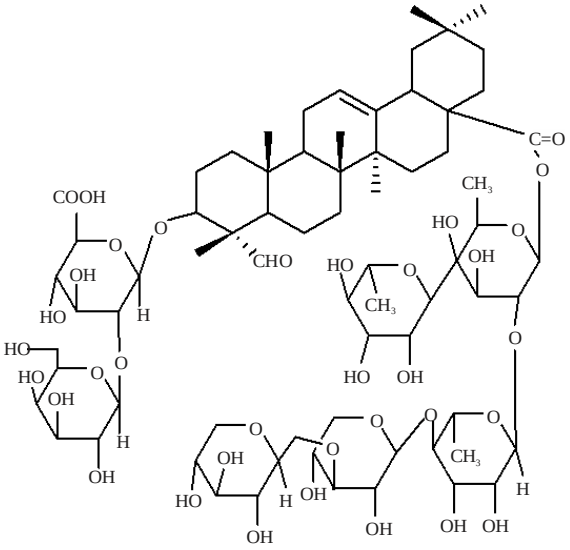


93 Gypsogenin

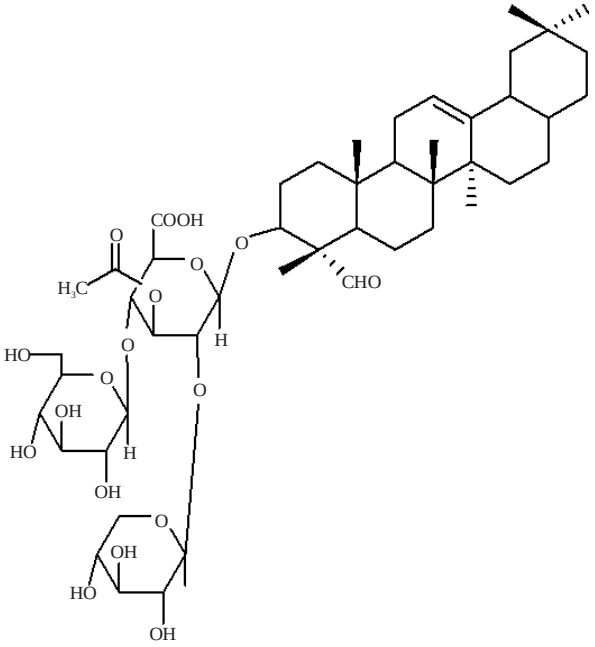
Fig. 1: Continue



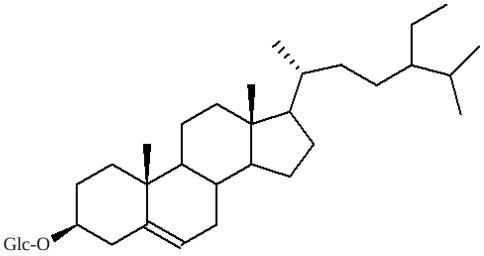
94 Goyasaponins I



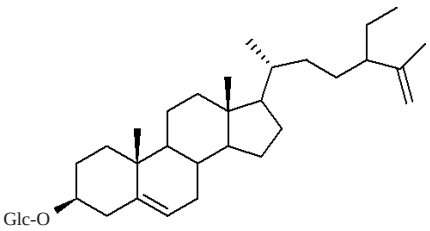
95 Goyasaponins II



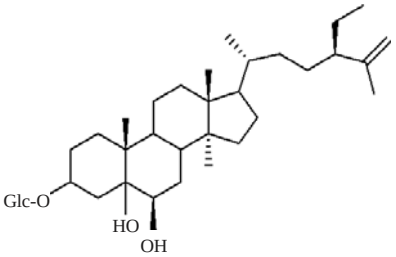
96 Goyasaponins III



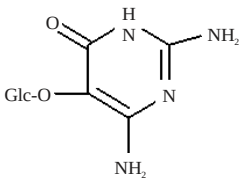
97 Sitosterol glucoside



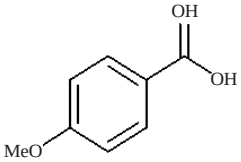
98 5,25-Stigmastadienol glucoside



99 24(R)-stigmastan-3β, 5α, 6β-triol-25-ene-3-O-β-glucopyranoside



100 Vicine



101 p-methoxy-benzoic acid

All = D-allopyranosyl, Glc = D-glucopyranosyl, Xyl = D-xylopyranosyl

Fig. 1: Chemical structures of phyto-constituents that are reported from *Momordica charantia*

Momordica charantia contains a diverse range of cucurbitacins like other vegetal curcurbits. Cucurbitacins represent a special class of compounds found exclusively among the members of Cucurbitaceae. The basic structure of a cucurbitacin (1) resembles a lanostane ring (2) except that the former bears a C-19 methyl group at C-9 rather than at C-10 as in the latter. Thus cucurbitacins are 19-(10α→9β)-abeo-10α-lanost-5-ene type systems. Most of the cucurbitacins found in *M. charantia* have an eight-membered branched side-chain at C-17. The side-chain is either saturated (3-5) or unsaturated (6, 7). A double bond is essentially present at C-5 that may shift to C-6 if C-5 is involved in epoxy ring formation. Additional double bonds may be present at C-23 (8-13) or C-24 (14-16). The C-19 methyl group found in cucurbitacins may get oxidized to an aldehyde, ketonic or carboxylic functionality. Cucurbitacins have one or more hydroxyl, keto, carboxyl, methoxy or acetoxy substitutions in their cyclic framework or in the side-chain. This has resulted in a greater diversity of both the structure and stereochemistry of cucurbitacins reported from *M. charantia* (17-20). Usually the cucurbitacins are tetracyclic, but some representatives have an extra epoxy ring due to formal cyclization between C-5 and C-19 as in goyaglycosides a-f and others (21-31). On the other hand, momordicosides represent a special group of cucurbitacins found only in *M. charantia* that have a C-19 methyl oxidized to an aldehyde group. Cucurbitacins in *M. charantia* are found either in glycosidic (25-32) or free form (33-53). In some cucurbitacins, a three-membered epoxy ring between C-5 and C-6 is formed (37-39). Polynorcucurbitacins have been also reported from *M. charantia* that may have a five-membered side-chain as in trinorcucurbitacins (34-36), three membered side-chain as in pentanorcucurbitacins (54-56) or no side-chain at all as in octanorcucurbitacin (57-60). Cucurbitacins with hydroxylation or methoxylation at C-7 and C-25 (61-70) are less common in *M. charantia*. Some of the constituents show exocyclic or endocyclic conjugated system (71-74). Still other members exhibit hydroxylation, alkylation, acetylation or glycosylation at one or more positions in cucurbitane framework (75-92). Besides cucurbitacins, *M. charantia* also contains triterpenoids (93-96), sterols (97-99), vicine (100) and p-methoxy benzoic acid (101).

PHARMACOLOGICAL REPORTS

Momordica charantia has a long history of human use in traditional medicine throughout the world. There is a plethora of reports of experimental and clinical evidences related to its different uses that are summarized below.

Antidiabetic and antihyperlipidemic activities: Charantin, an active fraction of *M. charantia*, when administered to normal rabbits has been reported to produce a gradual but significant fall in blood sugar level. However, in alloxan induced diabetic rabbits, the effects were more erratic. Pancreatectomy was found to reduce but not abolish the hypoglycemic effect of charantin indicating a dual mechanism of action[20]. Polypeptide-P, isolated from the fruits and seeds of *M. charantia*, showed a potent hypoglycemic effect when administered subcutaneously to gerbils and humans[22].

Aqueous extract of immature fruits of *M. charantia* has been shown to partially stimulate insulin release from isolated β-cell of obese-hyperglycemic mice[23]. Oral feeding of ethanolic extract of *M. charantia* to normal rats prior to glucose loading increased hepatic and muscle glycogen content while significantly lowered blood sugar levels[24]. Oral administration of acetone extract of fruit powder of *M. charantia* for 15-30 days to alloxan-induced diabetic rats lowered the blood sugar and serum cholesterol levels to normal range[25]. Handa *et al.*[21] found that vicine from the seeds of *M. charantia* on intraperitoneal administration caused a hypoglycemic response in normal fasting albino rats. The fruit juice significantly increased the number of β-cells in *M. charantia* treated animals when compared to untreated diabetic rats. The number of α-cells did not change significantly in *M. charantia* treated rats when compared with untreated diabetic rats[26].

Yibchok-Anun *et al.*[27] reported that protein extract from *M. charantia* significantly increased insulin secretion and increased glucose uptake in adipocytes. Acetone extract of whole fruit powder of *M. charantia* at dose levels of 25, 50 and 75 mg/100 g b.wt., lowered the blood glucose from 13.30-50% after 8-30 days treatment in alloxan-induced diabetic albino rats. Histological observations showed different phases of recovery of β-cells of the islets of Langerhans of pancreas[28]. Out of fourteen cucurbitane-type triterpene glycosides isolated from a methanol extract of *M. charantia* fruits, charantosides A-C were evaluated for α-glucosidase inhibitory effect, of which charantoside A showed moderate inhibitory activity against α-glucosidase[17]. *Momordica charantia* capsules in doses of 2000 mg day^{-1} demonstrated statistically significant improvement in fasting blood glucose as well as 2 hour postprandial blood glucose level[29].

Choudhary *et al.*[30] evaluated anti-hyperglycemic activity of fractionated *M. charantia* seed extracts in diabetic rats. Fasting blood glucose levels were evaluated before and after administration of different fractions (15 mg kg^{-1} b.wt.) of the seed extract. A soluble fraction of acid-ethanol extract of *M. charantia* after precipitation with ammonium carbonate

designated as MC-3 showed the maximum anti-hyperglycemic activity and reduced blood glucose levels significantly. Perumal *et al.*[31] evaluated the changes in urinary metabolite profile of the STZ-induced type 1 diabetic rats using *M. charantia* extract (100 and 200 mg kg^{-1} b.wt.). The results indicated that *M. charantia* was effective in lowering blood glucose level and also regulated the altered urinary metabolite profile.

Xu *et al.*[32] isolated a water-soluble polysaccharide (MCP) from the fruits of *M. charantia* and the its effect was evaluated in alloxan-induced diabetic mice at 100, 200 and 300 mg kg^{-1} b.wt. for 28 days. Results showed that fasting blood glucose level was significantly decreased, whereas, the impaired glucose tolerance was markedly improved in alloxan-induced diabetic mice. Raish *et al.*[33] investigated reno-protective nature of MCP by evaluating the anti-hyperglycemic, anti-hyperlipidemic and antioxidant proficiency in streptozotocin (STZ)-induced diabetic rats. The oral administration of MCP showed a significant normalization in the levels of markers of oxidative stress in the STZ-induced diabetic rats. The MCP treatment also illustrated a significant improvement in glutathione peroxidase, superoxide dismutase and catalase levels. Immunoblots of heme-oxygenase 1 and Nrf2 of MCP treated diabetic rats showed a significant up-regulation of both the proteins.

Anticarcinogenic activity: Kusamran *et al.*[34] evaluated the effects of *M. charantia* on the levels of phase I enzymes, which include cytochrome P_{450}, aniline hydroxylase and aminopyrine-N-demethylase and the phase II enzymes i.e., glutathione S-transferase in rat liver. It was demonstrated that bitter-gourd fruits contain compounds that act as phases I and II enzyme inducers and are capable of repressing some mono-oxygenases, especially those involved in the metabolic activation of chemical carcinogens. Ganguly *et al.*[35] reported skin papilloma prevention by aqueous extract of *M. charantia* fruits. The results suggested a preventive role of water-soluble constituents of *M. charantia* fruit during carcinogenesis, which is mediated possibly by their modulatory effect on enzymes of the bio-transformation and detoxification system of the host. The oxygen free radical scavenging activity of the juice of *M. charantia* fruits is also reported[36].

Wound healing activity: Sharma *et al.*[37] reported significant wound healing activity in animals treated with *M. charantia* extract compared to those who received the standard and control treatments. In excision wound model, *M. charantia* extract treated animals showed a significant reduction in wound area and period of epithelization. The extract treated animals showed faster epithelization of wound than the control. The wound healing activity of olive oil macerate of *M. charantia* was evaluated in linear incision and circular excision wound models created in the buccal mucosa of the rat. Olive oil macerate of *M. charantia* showed significant wound healing activity both in incision (45.1%) and excision (89.8%) wound models and demonstrated anti-inflammatory activity with the inhibition value of 31.3% at the dose[38] of 100 mg kg^{-1}.

Anti-inflammatory and analgesic effects: *Momordica charantia* fruit extract exhibits a dose dependent anti-inflammatory activity in carrageenan-induced paw edema in rats. The oral administration of *M. charantia* ethanolic extract showed 42.10% anti-inflammatory effect at dose 500 mg kg^{-1} b.wt. The fruit extract was also tested for analgesic activity in acetic acid induced writhing test and tail immersion test in mice. The oral administration of *M. charantia* extract significantly inhibited acetic acid induced writhing and tail immersion induced pain at dose 500 mg kg^{-1} b.wt.[39]. The anti-inflammatory and antiulcer potential of seeds of *M. charantia* have been attributed to the presence of antioxidant in it[40]. Methanolic extract of the seeds from unripe fruits of *M. charantia* has been shown to produce a marked dose-dependent analgesic effect in mice and a much weaker effect in rats by using different test systems for the two species[41]. Naloxone pretreatment failed to modify the analgesic response, suggesting that opioid receptors were not involved[42].

Hepatoprotective action: Bitter gourd juice and seed extract (10 mL kg^{-1} b.wt., daily for 30 days) exhibited hepatoprotective effects by elevating serum γ-glutamyl transferase and alkaline phosphatase enzymes[43].

Antiviral potential: *Momordica charantia* fruit extract is reported to inhibit the growth of *Herpes simplex* virus I[44] and human immunodeficiency virus I[45]. Increased T-cell count and a normalization of the CD4/CD8 ratio seemed to occur in three HIV positive patients given regular doses of *M. charantia* fruit juice[46].

Antipyretic effects: The ethanolic extracts of *M. charantia* fruit (500 mg kg b.wt.) showed antipyretic effect in a study that was carried out using yeast-induced pyrexia in rats. The antipyretic activity of *M. charantia* was postulated to be due to individual or combined action of bioactive constituents present in it[47].

Antimalarial and larvicidal activity: *Momordica charantia* was evaluated for antimalarial activities against different *Plasmodium* species. The study showed moderate *in vivo* activity of *M. charantia* extract against rodent malaria *Plasmodium vinckei petteri* and an excellent anitimalarial activity *in vitro* on *Plasmodium falciparum*[48]. *Momordica charantia* has shown good larvicidal activity against three breeding mosquito species: *Anopheles stephensi*, *Culex quinquefasciatus* and *Aedes aegypti*[49].

CONCLUSION

Momordica charantia is a rich source of chemically novel compounds and needs exhaustiue screening against new targets in future. This compilation of its phytochemical and pharmacological reports will help the researchers in dereplication and designing new investigational strategies. The biologically active cucurbitacins, momordicosides and steroidal glycosides from *M. charantia* are the main focus of this review.

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