Exploring the nutraceutical potential: Antioxidant and anti-inflammatory properties of *Momordica charantia*

Swapna Guda, Kalakumar Bharani, Anilkumar Banothu and Ravikumar Yadala

**Abstract**

*Momordica charantia*, commonly known as bitter melon, has been extensively utilized in traditional medicine for addressing various chronic inflammatory conditions, notably Diabetes mellitus. Many studies showed the potential of *Momordica charantia* in alleviating inflammation and oxidative stress, attributing its efficacy to its robust antioxidant and anti-inflammatory properties. The mechanistic insights reveal that these beneficial effects are primarily mediated through the down regulation of the NF-κB signaling pathway and the concurrent up regulation of the Nrf2 signaling pathway. Based on the study *Momordica charantia* as a promising therapeutic candidate for managing a spectrum of lifestyle-related diseases.

**Keywords:** *Momordica*, antioxidant, anti-inflammatory NF-Kb, Nrf-2

**Introduction**

*Momordica charantia* L. the plant being used for years in folk medicine with common as bitter melon or bitter gourd belongs to the family, Cucurbitaceae (Krawinkel & Kedig 2006) [2]. Being distributed widely in the areas Asia, South America and the African countries and also in the Caribbean and Amazon basin. The word *Momordica* in Latin implies as “to bite” due to the jagged leaf edges. Depending upon the size of the fruit, it has been divided into minima where fruit size is less than 5 cm. In contrary, it was categorized as maxima where fruit size is above 5 cm. *M. charantia* is generally cultivated for its fruit which is known for various medicinal properties (Basch et al., 2003) [3]. The bitter taste is because of the presence of curcurbitane glycosides which are nontoxic and named as momordicoside K, momordicoside L, momordicine I, and momordicine II (Basch et al., 2003) [3]. Various plant parts especially roots, tender twigs, flowers, fruits and seeds are commonly used as flavoring agents (Schartezzini and Speroni, 2000; Morgan & Midmore, 2002) [4, 5]. Immature fruits will be useful for culinary purpose, preparation of pickles and canned foods. In India, mostly in the culinary practice the fruits as well as the leaves are mostly used as treatment for diabetes, abdominal pain and for wound healing (Paul et al., 2009) [6]. Some people use leaf juice against for diabetes. It contains diuretic, laxative and anti-helminthic properties.

**Chemical constituents of Momordica charantia**

*Momordica charantia* exhibits many medicinal uses, as an anti-diabetic, hypercholesterolemia, hypotriglyceridemic, hypotensive agent, to boost the immune system as an immunostimulant, and even have the anti-viral, anti-inflammatory, antioxidant, antibacterial, anthelmintic, antimutagenic, anti-ulcer, anti-leukemic and also known for its insecticidal properties that were identified in different parts of *M. charantia* (Tan and Gan, 2016) [7]. The potential effects are greatly attributed to the Phytoconstituent chemicals present in all parts of MC and more specifically in fruit and seed such as flavonoids, steroids, saponins, glycosides, polysaccharides, fatty acids, alkaloids, triterpenoids, amino acids, essential oils. For management of body weight and in regulating the lipid metabolism MC contains the vital agents such as Ribosome-Inactivating Proteins (RIPs), charantin, polypeptide-p and vicine henceforth used for the treatment of hyperglycaemia (Li et al., 2015) [42].

**Anti-oxidant effects of Momordica charantia**

Perumal et al. (2021) [9] reported many compounds with the antioxidant properties which include 3- malonylmomordin C, goyaglycoside G ascorbic acid, quer-cetin 3-O-glycoside,
kuguacin H, brevifolin carboxylic acid cucurbitacin E, margarolic acid. Chokki et al. (2020)\(^{10}\) reported that MC extract contains Chlorogenic acid, daidzein, epicatechin, rutin, quercetin, naringenin, genistein and naringin, as polyphenol compounds and the extracts with ethyl acetate exhibited inhibition against the enzyme α-amylase. Jiang et al. (2020)\(^{11}\) reported the increased activity of the enzymes SOD and CAT and the decreased malonaldehyde (MDA) levels in the pancreatic and liver tissue of the rats 4 weeks after administration of MC saponins (MCS) indicating that these MCS prevented the damage caused because of oxidative stress by enhancing the activity of antioxidant enzymes and reducing the lipid peroxidation. Perez et al. (2019)\(^{17}\) reported that the non-polar extracts of MC has got more inhibitory effect on the enzymes α-glucosidase and α-amylase, with pronounced inhibitory activity observed with chloroform and hexane extracts for α-glucosidase and the medium polar extracts inhibited α-amylase. Gupta et al. (2019)\(^{13}\) reported dose dependent inhibition of the enzyme pancreatic lipase from the ethanolic extract of MC. Chanda et al. (2019)\(^{14}\) reported positive correlation between phenolic content of ethyl acetate fraction of MC fruit extract and its pancreatic enzyme lipase inhibitory activity statistically, clearly demonstrating the role of phenolic compounds for higher inhibitory activity.

Yang et al. (2018)\(^{23}\) in a study on murine macrophages reported that *Momordica charantia* reduced the expression levels of iNOS and cyclooxygenase-2 (COX-2), suppressing NF-κB, and activator protein-1 (AP-1) activity. Bai et al. (2007)\(^{25}\) in an in vivo study on high fat fed mice reported that the supplementation with MC powder lowered the systemic inflammation in obese mice by regulating the genes involved in inflammation and inturn reducing the serum levels of TNF-α and IL-6. Yang et al. (2018)\(^{23}\) reported that supplementation of MC extracts in TNF-α treated mice reduced the intercellular adhesion molecule-1 expression with decreased the PI3K/Akt/NF-κB/IκB. Kim et al. (2018)\(^{24}\) reported that pretreatment of neuroblastoma cells in an in vitro study with MC extracts was found to regulate the cytotoxic oxidative stress which was induced by H2O2 by enhancing the intracellular scavenging activity and by reducing the H2O2 -induced activation of the vital signaling pathway JNKs, p38, and ERK1/2 MAPK. MC fruit extract significantly reduced the levels of SGOT and SGPT and also up regulated the genes expression encoding for the antioxidant enzymes SOD, CAT and GPx (Malekshahi et al. 2019)\(^{25}\). Adelusi et al. (2021)\(^{26}\) identified two vital compounds of MC (Catechin and Chlorogenic acid) which when bound to the Keap1 kelch domain and act as potential Nrf2 signalling activator through the downregulation of its Keap1 repressor during the in-silico research findings.

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**Fig 1:** Mode of action of *Momordica charantia* (Bortolotti et al., 2019)
Wang et al. (2017) [27] reported that the polysaccharide and saponins are the major bioactive substances which aid in significant improvement in the antioxidant capacity by enhancing the level of SOD and reducing the level of MDA and alleviate the STZ-induced tissue damage of kidney in the diabetic nephropathy condition by reducing the level of serum creatinine.

Anti-inflammatory effects of Momordica charantia

*Momordica charantia* contains PPARα and PPARγ activators which are known for maintaining the lipids in the blood and also exhibit anti-inflammatory activity (Ciou et al., 2014) [28]. The mechanisms exhibited at the molecular level is by inhibition of cytokines secreted by monocytes following PPARγ activation (Chao and Huang, 2003) [77] and interfere with the signaling of messages for NF-κB, by inhibiting the expression of vital inflammatory genes which code for IL-1, IL-2, IL-6, IL-8, TNF-α and matrix metalloproteinase (MMPs) (Mukherjee et al., 1994) [29]. PPARγ also reduces the activity of iNOS by inhibiting NFkB the transcription factor, thus alleviating inflammation (Ricote et al., 1998) [37]. Similarly, *Momordica charantia* significantly reduces the mediator of inflammation PGE2 by decreasing the expression of COX-2 protein (Chao et al., 2014) [28]. *Momordica charantia* is mainly enriched with the vital flavonoid compounds such as charantins, and an increase in the anti-inflammatory properties noticed in *Momordica charantia* might be attributed to the presence of major active compounds such as charantosides (Abas et al., 2014) [31]. Anti-inflammatory activity noticed in the condition might be attributed to the production of 1, 25 (OH) D₃ during vitamin D metabolism and also *Momordica charantia* treatment lowered NF-κB, iNOS, COX-2, IL-6, IL-23, IL-1β, TNF-α and IFN-γ mRNA and protein levels (Shivanagoudra et al., 2019 and Acar et al., 2020) [17, 32]. *M. Charantia* extracts were found to lower the systemic inflammation in the body mainly by lowering the levels of TNF-α and IL-6 in the serum levels (Bai et al., 2007) [22]. The phytoconstituents present in the fruit effectively inhibited the mediators of inflammation, viz., PGE2 and nitric oxide (NO) (Hsu et al. 2011; Hsu et al. 2012 and Leung et al. 2009) [33, 34, 35]. Activation of PPARγ can attenuate the production inflammatory mediators like TNF-α, IL-6 and IL-1β (Hanada and Yoshimura, 2002) [36]. PPAR γ also can reduce the iNOS enzyme activity by inhibiting the activation of transcription factor NF-κB, henceforth alleviating the inflammation (Ricote et al. 1998) [37]. Bitter melon treatment reduced the production of pro-inflammatory cytokines and other substances and alleviate the inflammatory responses (Chao et al. 2014) [28]. Bitter melon treatment in IL-1β-treated hepatocytes deactivated the expression of iNOS protein. The extracts of bitter melon decreased the levels of iNOS mRNA indicating the inhibition of expression of the iNOS gene at the transcriptional level or later and also decreased the levels of mRNAs which code for pro-inflammatory cytokines (TNF-α and IL-6) and chemokines (CCL20 and CX3CL1). Also, suppressed the expression of TNF-α and IL-6 mRNA which play major role in chronic liver injury and inflammation. The cucurbitane-type triterpenoids, may be responsible for the anti-inflammatory effects of bitter melon (Dwijayanti et al. 2019) [38].
Table 1: Bioactive components, distribution and mode of action in *Momordica charantia*

<table>
<thead>
<tr>
<th>Major Phytoconstituent</th>
<th>Biological Function</th>
<th>Part of the plant</th>
<th>Reference</th>
</tr>
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<tbody>
<tr>
<td>Polysaccharides</td>
<td>Antioxidant, Neuroprotective, immune stimulant, anti-diabetic, anti-tumorigenic</td>
<td>Vital plant parts</td>
<td>Xu et al. 2015 [59], Zhang et al. 2016 [40]; Deng et al. 2014 [41]; Duan et al. 2015 [42]; Cai et al. 2010 [43] and Zhang et al. 2008 [40]</td>
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<tr>
<td>Lipids</td>
<td>Antioxidant, Antitumor</td>
<td>Seed, flesh</td>
<td>Tsuzuki et al. 2004 [52]; Dhar et al. 2007 [51] and Suzuki et al. 2010 [53].</td>
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<tr>
<td>Terpenoids</td>
<td>Antioxidant, Anticancer, hypoglycemic, anti-diabetic, cancer chemoprevention</td>
<td>Stem, leave, fruit</td>
<td>Akihisa et al. 2007 [54]; Liu et al. 2010 [56]; Agrawal, and Beohar, 2010 [55]; Chou et al. 2015 [57].</td>
</tr>
<tr>
<td>Saponins</td>
<td>Antiviral, hypolip idemic, antihyperglycaemic,</td>
<td>Fruit, root, seed</td>
<td>Hsiao et al. 2013 [58]; Han et al. 2008 [59]; Xia et al. 2007 [60]; Chang et al. 2004 [61]; Zhang et al. 2011 [62] and Patel et al. 2010 [63].</td>
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<tr>
<td>Sterols</td>
<td>Antimicrobial</td>
<td>Pericarp, fruit</td>
<td>Saeed and Tariq, 2005 [68]; Begum et al, 1997 [69]; Guevara et al, 1989 [70].</td>
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Table 2: Bioactive compounds of *Momordica charantia* under different groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Compounds</th>
<th>Distribution</th>
<th>Reference</th>
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<tbody>
<tr>
<td>Cucurbitane Triterpenoids</td>
<td>Charantin &amp; III, Karavilagenin A, B, C, D, E, saponins (triterpenoid glycosides), Goya saponins, saponins such as diosgenin</td>
<td>Leaves &amp; roots</td>
<td>Ullah et al. 2011 [72]; Li et al. 2015 [52]; Ingle &amp; Kapgate 2018 [73]; Ummi et al. 2018 [74]; Shubha et al. 2018 [75]; Mahwish et al. 2018 [76].</td>
</tr>
<tr>
<td>Phytosterols</td>
<td>campesterol, β sitosterol, decontinone, ergosterol peroxide, clerosterol, stigmasterol</td>
<td>Fruit</td>
<td>Ullah et al. 2011 [72]; Ummi et al. 2018 [74]; Shubha et al. 2018 [75]; Kim et al. 2013 [75].</td>
</tr>
<tr>
<td>Alkaloids</td>
<td>Fruits, Leaves &amp; Seeds</td>
<td>Mahwish et al. 2018 [76]; Shubha et al. 2018 [71]; Ingle &amp; Kapgate 2018 [73].</td>
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</table>

Conclusion

*Momordica charantia* which is been most commonly used since ages in traditional folk medicine for treating various chronic ailments associated with metabolic disorders viz., Diabetes mellitus. Treatment with *Momordica charantia* could abrogate the changes observed in inflammation and oxidative stress owing to its antioxidant and anti-inflammatory potential mainly achieved through down regulating of the nuclear factor-κB signaling pathway and up regulating the Nrf2 signaling pathway. Therefore, *Momordica charantia* could act as a promising avenue in the treatment of various life style diseases.

References


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