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Charantin: An important lead compound from *Momordica charantia* for the treatment of diabetes

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Abstract
The development of effective and safe anti-diabetic agent is still a major challenge for modern scientific research. Traditionally fruit juice of *Momordica charantia* has been used for treatment of diabetes for centuries. Charantin, a natural steroidal glycoside present in the fruits of this medicinal plant, has been reported to possess potential hypoglycemic activity. However, this phytoconstituent has not been explored yet clinically to treat diabetes. This review summarizes the chemistry, biological activity and reported analytical methods for charantin, a bioactive compound present in *M. charantia.*

Keywords: Charantin, Diabetes, *Momordica charantia*, steroidal glycoside

1. Introduction

Diabetes or diabetes mellitus (DM) is chronic metabolic diseases characterized by high blood sugar levels caused either due to inadequate production of insulin or due to inability of body cell to respond to insulin [1]. As per WHO, currently over 382 million people are affected globally and diabetes will emerge as 7th leading cause of death in 2030 [2]. There are many synthetic antidiabetic drug molecules available for the management of DM but these molecules are associated with numerous undesirable side effects. Hence there is an obvious need for search for safe and effective drug moieties for the treatment of DM. Herbal drugs are effective, cheap and are considered to be safe as they possess fewer side effects as compared to synthetic drugs [3]. In traditional system of medicine, many medicinal plants have been identified for their hypoglycemic activity with potential use in DM. Important medicinal plants with hypoglycemic activity include *Azadirachta indica, Allium sativum, Ficus bengalensis, Lagerstroemia speciosa, Momordica charantia, Syzygium cumini,* etc [4, 5]. Principal leads have been identified which are responsible for hypoglycemic activity of these plants [6]. This review describes phytochemistry, isolation procedure and analytical methods for charantin, a bioactive compound from *Momordica charantia.*

2. *Momordica charantia*

M. charantia (Family: Cucurbitaceae) is of the medicinal plants with hypoglycemic activity being studied extensively. It is a climber widely cultivated as food in Asia, Africa and South America. It is also found all over India and cultivated upto an altitude of 1500 m. The word *Momordica* is derived from the Latin word *Mordeo* which means to bite and the species name is derived from Greek word and it means beautiful flower. Fruit of this plant is known as bitter melon, bitter gourd, balsam pear or African cucumber [7, 8]. Fruits are traditionally used for hypoglycemic activity. Apart from fruits, leaves and seeds are also used [9]. Several studies on different animal models also proved the hypoglycemic activity of fruits [10-16]. Main phytoconstituents present in fruits are charantin, momordicin, momordin, stigmasta-5, 25-dien-3-β-O-glucoside, β-sitosterol-β-D-glucoside, momordicoside G, momordicoside F1, momordicoside F2, momordicoside I, momordicoside K, momordicoside L, etc [17-19].

3. Charantin

Charantin is steroidal glycoside and exist as equal mixture of stigmasterol glucoside and β-sitosterol glucoside (Figure 1 and 2). It has got blood sugar lowering property equivalent to insulin [20].

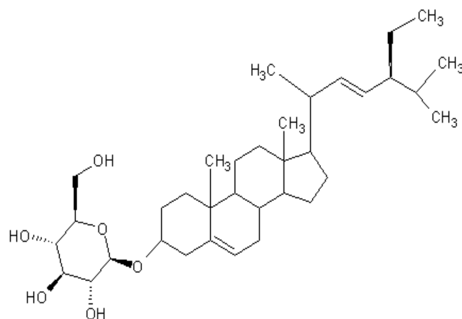

Fig 1: Structure of stigmasterol glucoside

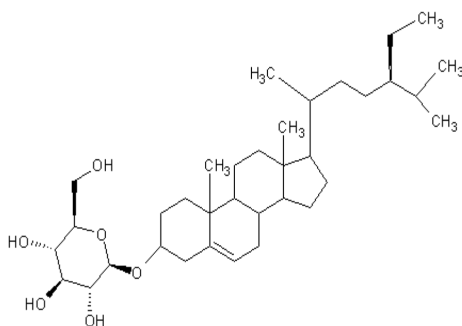

Fig 2: Structure of β-sitosterol glucoside

3.1. Description: It is a white crystalline, neutral and tasteless compound.

3.2. Solubility: Solubility of charantin is challenging as the molecule of steroidal glycoside consists of both aglycone part and sugar moiety. The presence of steroidal backbone as aglycone part increases its solubility in non-polar solvents such as chloroform and dichloromethane whereas the presence of glucose moiety makes it slightly soluble in polar solvents such as ethanol or methanol. Charantin is soluble in ether [20].

3.3. Melting Range: 266-268 ^{0}C

3.4. Phytochemistry: With Libermann-Burchard test, charantin gives violet colour changing to blue, green and yellow. On hydrolysis with acid it produces glucose and sterol [21]. It gives violet- blue colour and pink colour on spraying with anisaldehyde sulphuric acid reagent and vanillin sulphuric acid reagent, respectively.

3.5. Pharmacology [21]

3.5.1. Hypoglycemic activity: Charantin isolated from fruits of *M. charantia* was tested for its hypoglycemic activity. In fasting rabbits, it gradually lowered blood sugar within one to four hours and recovered slowly to initial level. At an oral dose of 50 mg/kg, blood sugar level was declined by 42% at the 4th hour. The average blood sugar fall during 5 hours was 28%. Charantin was found to be more potent than tolbutamide however both compounds produced similar pattern of blood sugar change. The hypoglycaemic activity of charantin in depancreatixed cats was less, but abolished, indicating a pancreatic as well as extra-pancreatic action.

3.5.2. Cardiovascular effects: Effect of charantin on cardiovascular system was studied. At the dose of 800 mg/kg, 5-10% of blood pressure lowering of anaesthetized cat was observed. The contraction of isolated heart of frog was increased at dose of 5-10 mg and the same dose was effective to terminate action of acetylcholine.

3.5.3. Anti-sialogogue activity: Charantin at dose of 10-15 mg/kg delayed the onset of tremors but did not affect salivation produced by tremorine.

4. Isolation of charantin

Few attempts have been made to extract and isolate charantin from fruits of *M. charantia* using various chromatographic techniques.

Effect of different solvents (acetone, dichloromethane, ethanol and water), solvent composition (ethanol and water), solvent flow rate and temperature on extraction efficiency of charantin was evaluated. Ethanol was found to be the most effective solvent for extraction of charantin. Yield was increased with increase in temperature. Purification of charantin was done by treating extract using 50-70% of methanol solutions and pure hexane [20]. T.B. Ng *et al.* isolated charantin from seeds of *M. charantia* by affinity chromatography, ion-exchange chromatography and gel filtration chromatography. Seeds were extracted with 10 mM Tris-HCl (pH 7.2). The extract was filtered and chromatographed on affinity column DEAE-cellulose column, Affi-gel Blue gel and then by ion-exchange chromatography on Mono S column to get pure charantin [22]. Charantin was extracted by mixing dry powder of fruits with water. The mixture was boiled and filtered. Different amounts of PEG, K_2HPO_4 and ethanol were added to various amounts of water extract and an aqueous two-phase system was prepared. The system was vortexed, centrifuged and charantin-containing salt-rich layer was extracted with 95% ethanol. The ethanol extract thus prepared was kept overnight at 4 ^{0}C and salt was allowed to precipitate. Precipitates were removed and amount of charantin was estimated by UV spectrometry [23]. Charantin was isolated from dried fruits by successive extraction with petroleum ether (60-80 ^{0}C) and 80% ethanol. The ethanol extract was concentrated to a small volume and basified with KOH. After 48 h, the ethanol solution was diluted with water and extracted with ether. The ether extract was washed with water, HCl and again with water. The aqueous and acid washings were discarded. The ether layer was distilled off and the residue was recrystallized several times using 95% ethanol to get charantin [24].

5. Analysis of charantin

5.1. HPLC: Chanchai estimated charantin by HPLC using C18 Hypersil column (300 mm X 3.9 mm, 10 µm) and mobile phase consisting of methanol: water (100: 2, v/v) at flow rate of 1.0 ml/min. Detection was carried out at 204 nm. Charantin eluted at retention time of 8.1 min. [25] Charantin was determined using a C-18 Inertsil ODS-3 column (250 mm X 4.6 mm, 5 µm) and mobile phase composed of methanol: water (100:2, v/v). Flow rate of mobile phase was 1.0 ml/min and detection was carried out at 204 nm. Retention time of charantin was approximately 12.0 min [20, 26].

5.2. HPTLC: Methods have been reported for TLC and HPTLC studies of charantin.

Charantin was isolated and its TLC study was carried out using methanol: benzene (2:8, v/v) as mobile phase. Rf value of charantin was found to be 0.45 [24]. To study the impact of boiling, % of charantin was estimated in bitter melon fruits by HPTLC using Silica gel plates as stationary phase and chloroform: methanol: water (1.5:6:2.5, v/v/v) as mobile phase. Charantin eluted with Rf of 0.40 [27]. Ahamad *et al.* determined charantin in fruits and herbal formulations containing *M. Charantia* using silica gel 60 F254 plates as

stationary phase and toluene: ethyl acetate: methanol: formic acid (68:20:10:02, v/v/v/v) as mobile phase. Detection was carried out at 525 nm after derivatization with anisaldehyde sulphuric acid reagent. Charantin eluted with Rf value of 0.71 [28]. Charantin was quantitated in ethanol extracts of leaf and fruits of *Momordica tuberosa* and *Momordica dioica* using silica gel 60f 254 TLC plates as stationary phase and benzene: methanol (8: 2, v/v) as mobile phase. At 536 nm, Charantin was detected with Rf value of 0.31 [29].

6. Conclusion

Nowadays, natural products are acquiring substantial importance for the treatment of diabetes. Recent advances in scientific research have proved the role of *M. charantia* for the management of diabetes. Charantin is also being investigated as bioactive principle for hypoglycemic activity. However, there is need to evaluate this natural compound clinically. Substantial clinical data needs to be generated to establish hypoglycemic potential of this compound and to support emergence of safe and effective antidiabetic agent. Additionally, newer techniques should be adopted for cultivation of plant materials which are rich in charantin. Cost effective synthesis procedures and purification process needs to be developed. Effective isolation techniques which can isolate stigmasterol glucoside and β-sitosterol glucoside distinctly needs to be established. Similarly, newer analytical methods should be developed with ability to resolve these compounds. The reported analytical methods could detect charantin as single component but the quantities of stigmasterol glucoside and β-sitosterol glucoside can vary in different plant materials. None of the reported analytical methods could resolve and quantitate these steroidal glycosides in single run. Principles of novel drug delivery systems should be used for development of nanoparticles, microspheres or other novel formulations of charantin and these formulations should be evaluated for their efficacy. Improved efficacy supported by sufficient clinical data for charantin can bring this plant-based molecule to the lead of hypoglycemic agents for the management of diabetes.

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