Journal of Pharmaceutics and Drug Research
JPDR, 2(2): 74-77
www.scitcentral.com

ISSN: 2640-6152

Mini Review: Open Access

A Comparative Study of Manosrin a Triterpene Saponin from *Anisopus mannii* with Conventional Hypoglycaemics: Mini Review

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Received November 25, 2018; Accepted November 27, 2018; Published April 06, 2019

ABSTRACT

Diabetes mellitus is one of several diseases ravaging the African sub-continent. Research on *Anisopus mannii* a traditional medicinal herb of Nigerian origin yielded a new hypoglycemic compound Manosrin a Triterpene saponin. The mechanism of action was observed to be Thiazolidinedione like and it shows promise as a novel hypoglycemic compound. This article compares the mechanisms and demerits of conventional hypoglycemic compounds in with manosrin. It puts manosrin as a compound of promise towards arresting the DM pandemic.

Keywords: Manosrin, *Anisopus mannii*, Hypoglycemic, Fluidity

INTRODUCTION

The discovery of medicinal plants from the personal effects of the 'ice man', whose body was frozen in the Swiss Alps for over 5,300 years [1], became a major evidence to support the traditional use of plant (herbs) by man for medicine long before the ice age. Though the air was still cloudy about how the concept of traditional medicine was born, the various cultures of the world had somewhat similar accounts. The African story is linked to the supernatural and some ancient wisdom, and of course folk lore. Various ailments had different methods of treatments ranging from the use of herbs, salts, animal parts and sacrifices to the gods. In some cases, plant parts or exudates which resembles a part in humans or secretions were used as medicines [2].

The prevalence of several diseases long ago in the African subregion of West Africa, such as Diabetes mellitus, has made its debut in contemporary African society as a disease of affluence, change in life style and heredity [3].

DIABETES AS A SPECIAL CASE STUDY

Available evidence suggests that Diabetes mellitus is lowest in rural areas of developing countries, and is highest in certain ethnic groups who follow or adopt perceived 'western lifestyle' [3]. The understanding of Diabetes mellitus, moved from testing on ant hills to handy devices, from presumed attacks by evil spirits or witches to understanding the scientific basis and symptoms of the disease alongside mechanism of treatment methods based on the pathophysiological aspects. However, several studies evidence opined that Diabetes mellitus occurs as a result of the interplay between genetic disposition of and lifestyle of an individual [4].

CONVENTIONAL HYPOGLYCAEMIC DRUGS AND THEIR SIDE EFFECTS

Currently five groups of oral hypoglycaemic agents are among the most popular being prescribed for Diabetes mellitus patients. The introduction of new drugs may possibly render the achievement of better glycaemic control with drug therapy. However, in instances of renal failure, patients are cautioned, while a host of them are to be avoided altogether [5]. These groups of drugs are designed to do the following: i) Act by enhancing the production of insulin (Sulfonylureas and incretins); ii) Enhance peripheral insulin action (thiazolidinediones); iii) Inhibit hepatic glucose production (Metformin); iv) Slow intestinal absorption of glucose alpha-glucose inhibitors).

Apart from the effects that are encountered as a result of the overdoes and under dosage of insulin, treatment with human

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Citation: Zaruwa MZ. (2019) A Comparative Study of Manosrin a Triterpene Saponin from *Anisopus mannii* with Conventional Hypoglycaemics: Mini Review. J Pharm Drug Res, 2(2): 74-77.

or animal insulin have been observed to produce anti bodies in patients [6]. Some incretins on the other hand are said to be responsible for memory loss, sleep apnoea and reduced visual acuity [7]. The efficiency of sulfonylureas diminishes with time, usually owing to progressive β-cell impairment and cardiovascular problems [8]. Significant increase in body weight and some levels of hepatotoxicity was reported with sulphonylureas [9]. The α-glucosidase inhibitors cause drop in parked cell volume (PCV), which is linked to reduction in hemoglobin [10]. The most serious side effect with Biguanide is the occurrence of lactic acidosis [11], while the prolonged use and higher doses are associated with increased incidence of Vitamin B12 deficiency [12] among others.

MEDICINAL PLANTS AS ALTERNATIVE SOURCES OF NEW COMPOUNDS

The prevalence of Diabetes mellitus among local communities in the developing countries has been met with alternative medicines such as *Mormodica charantia* [13], *Glycyrrhiza glabra* [14], *Platycodon radix* and *Bellis perennis* [15], *Bridellia ferruginea* [16], *Leptedenia hastata* (Pers) Dec'ne. [17], *Anisopus mannii* [18], just to mention a few. Though orthodox medicines which complimented it helped to create a threshold of stability in the form of reduced death rate leading to what is today referred to as 'population explosion'.

Anisopus mannii subfraction extract: Manosrin (triterpene saponin)

The crude extract of *A. mannii* was reported to be non-toxic to diabetic animal models; it showed anti-inflammatory, analgesic, anti-cholesterolemic and antibacterial properties [19]. These attributes fit a plausible candidate for scrutiny as source of a good Diabetes mellitus drug. The isolation of Manosrin (3,23,28-Trihydroxy-12-oleanen-3-O-(β-D-glucopyranosyl-(1,6)-β-D-glucopyranosyl-(1,6)-β-D-xylopyranosyl)-28-O-β-D-glucopyranosyl-(1,6)-β-D-glucopyranoside) [20] chatted a new course for Diabetes mellitus treatment, after 1,7-naphthyridine alkaloid (anisopusine), 5-α-hydroxy-lup-20(29)-en-3-β-yl-eicosanoate, (6)-gingerdione, (6)-dehydrogingerdione and ferulic acid [21] were isolated from same. Manosrin, a Triterpene Saponin, previous studies showed that, it suppresses cholesterol absorption [22], inhibit the action of enzymes responsible for the synthesis of cholesterol [23], modulate mammalian immune system [24], improve anti-inflammatory and blood circulation [25], anti-carcinogenic [26], hyperlipidemic [15], hyperglycemic [27] and inhibits intestinal α-amylase [28] among others. The strong wound healing and other properties [29] attributed to these compounds is linked to the 3-O-glucoronide moiety and the 28-carbonyl group of the oleanolic acid glucoside. The said oleanic acid constitutes the core of new compound, manosrin **(Figure 1)**.

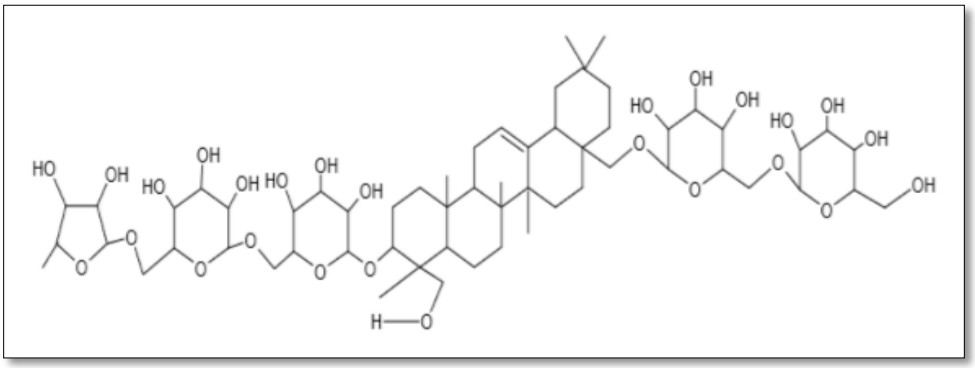

Figure 1. 3,23,28-trihydroxy-12-oleanen-3-O-(β-D-glucopyranosyl-(1,6)-β-D-glucopyranosyl-(1,6)-β-D-xylopyranosyl)-28-O-β-D-Glucopyranosyl-(1,6)-β-D-glucopyranoside (Manosrin).

MECHANISM OF MANOSRIN ACTION AND ITS MERITS

Results from earlier studies on the hypoglycemic effect of manosrin triggered speculations about the possible modus operandi of the active principle to be insulin enhancer (Thiazolidinedione action), a fasting blood glucose (FBG) suppressor in the diabetic mice [20]. Though the effect of the pure compound could be said to suggest alternative mechanism in addition to that which was earlier speculated, the sugar moiety in manosrin (hexose pentose) can be easily detached from the triterpene in mammalian gut by intestinal microflora [30] and thus inserted into cell membrane, modifying its molecular arrangement, thus affecting the fluidity [30]. This explains the hypoglycemic effect observed in the diabetic model, whereby the fluidity enhanced blood glucose entry into the cells for metabolism. The threshold dose with desired hypoglycemic effect in the Diabetes mellitus model was between 3.2 and slightly below 32.0 µg/kg above which the animals exhibited hyperactivity possibly as a result of the drop in FBG levels which can be said to be drastic [31], considering the time range. The drastic drop in FBG levels is due to gastric emptying and dopamine stimulation, leading to the stimulation of dopamine 2 receptors [32,33], hence the observed hyperactivity.

CONCLUSION

The discovery of manosrin from *A. mannii* as an addition to the already existing group of hypoglycemic compounds, has among others added advantage over existing hypoglycemic compounds, as a result of the simplicity of it mechanism of action and less side effect. This should serve as pointer to the promise of wonder drugs still waiting to be discovered from traditional medicinal plants of African origin. Though the compound compares with Glibenclamide in terms of percentage hypoglycemia, its modus operandi was more of thiazolidinedione. Therefore, Diabetes mellitus epidemy sounded by global health concerns with regards to Diabetes mellitus in developing countries may be checked if Manosrin and other compounds would be used therapeutically.

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