

## **Picralima Nitida Seed Oil I: Hypoglycemic Activity**

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### **ABSTRACT:**

The study aims to evaluate the blood sugar reduction activity of seed oil extracted from the seed of *Picralima nitida* and to compare its intraperitoneal and oral administration with that of seed extract and glibenclamide administered orally. The seed oil given intraperitoneally at dose levels of 1.0 and 0.25 ml/kg produce an initial increase in blood glucose that started resolving after three hours. The dose level of 0.125 ml/kg, however, did not produce this initial increase and had maximum blood sugar reduction of 20.1 % after six hours. The seed oil administered orally at 2.0 ml/kg gave a consistent reduction in blood glucose level with a maximum of 32.9 % of baseline occurring at the sixth hour. The seed extract at 500 mg/kg and glibenclamide at 0.07 mg/kg produced blood sugar reductions of 13.2 and 24.3 % respectively. The findings indicated that seed oil has a better blood sugar reduction activity when administered orally than when administered intraperitoneally. It also performs better than the seed extract and glibenclamide when administered orally.

**Key words:** *Picralima nitida*; seed oil; hypoglycemic activity.

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### **INTRODUCTION:**

Herbal drugs are receiving increasing patronage from dwellers all over the world. Ease of availability, affordability, and wide spectrum of activity has been the driving force towards their usage. Herbal drugs are less toxic with fewer side effects as compared to synthetic drugs. [1]

The plant, *Picralima nitida*, has provided drugs used in the treatment of many diseases. Extracts of the plant have been used in the treatment of pathogenic diseases [2], protozoan infections [3] and non pathogenic diseases. [4] Diabetes mellitus is a major endocrine disease that is treated with the extracts of the plant. [5] Extracts from various

parts of the plant including seed, stem bark, and rind have been used for this purpose. However, there is paucity of literature on the anti-diabetic activity of oil obtained from the seed. In this research work, therefore, the seed oil is administered through oral and parenteral routes and evaluated for hypoglycemic activity. This will enable a holistic utilization of the plant.

## **MATERIALS AND METHODS:**

### **Processing of seed**

The pod was washed with distilled water, dried with a clean disposable paper tissue and dissected longitudinally to expose the various inner components. The seeds embedded within the mesoderm were removed and allowed to dry at room temperature (27 °C). The testa were hand-peeled and further drying of the cotyledons was done at 40 °C until they turned dark brown and hard. Pulverization into coarse particles using a manual grinder (Corona model, Mexico) was performed. Further size reduction was done manually in a porcelain mortar. The resulting powder was screened through a 0.25 mm sieve and packed in an airtight glass container.

### **Extraction of seed oil**

The seed powder was macerated in n-hexane in a ratio of 1:3 for twenty-four hours with intermittent agitation. The extract was filtered using suction pump. The n-hexane was allowed to evaporate in an oven at 40 °C. The resulting oil was poured in an airtight amber-coloured glass container and stored in a refrigerator until required for use. The defatted seed powder was thereafter extracted with ethanol (95 %, BDH England) in a ratio of 1:5. Maceration was allowed to continue for twenty-four hours with occasional agitation. The supernatant was decanted off and filtered through suction pump using Watman filter paper (No 1). The resulting filtrate was poured into a stainless steel tray and allowed to dry in an oven at 40 °C. The resinous extract obtained was packed into a clean dried wide mouthed glass container and stored in a refrigerator.

### **Phytochemical analyses**

The seed extract was analyzed phytochemically using standard methods [6] for the presence of secondary plant metabolites.

### **Conditioning of animals**

Wister rats weighing between 250-300 mg were housed in cages for two weeks at room temperature (27 °C). The animals were fed *adlibitum* with growers mash chicken feeds

and allowed free access to water. Prior to drug administration, they were removed from feedlot and starved for two hours.

### **Hypoglycemic evaluation of seed oil**

The oil was administered to the animals using intraperitoneal (IP) route. Oral administration (PO) was done using an oral intubation set.

Blood glucose was monitored at baseline time and at 1-, 2-, 3-, 4-, and 6-hour intervals after administration of the drugs. One touch glucometer (Life scan, USA) was used for the blood glucose measurements. The drugs were administered to sets of rats with four rats per set. Seed oil was administered at varying doses of 0.125 ml/kg, 0.250 ml/kg and 1.00 ml/kg through IP route and 2.0 ml/kg orally. The seed extract which is known to be hypoglycemic and glibenclamide are used as positive controls. Exactly 1.00 ml/kg of normal saline was administered IP to another set of rats, to serve as one of the controls.

### **RESULTS AND DISCUSSIONS:**

The average weight of seeds per pod is 100.5 g while the average weight of a pod is 866.7 g. The extract from the powdered seed gave 9.50 % of the powder while the oil extracted from the seed powder was 1.77 % of the powdered seed.

Phytochemical analyses of seed extract of *P. nitida* show that saponins and other glycosidic compounds occur in the seeds. There are also the presence of tannins, alkaloids, terpenoids, steroids, resins, reducing sugars and carbohydrates. The seed extract is moderately acidic with a pH of 4.5. Hypoglycemic effects of seed oil of *P. nitida* administered intraperitoneally (IP) on normoglycemic Wister rats are presented in Table 1.

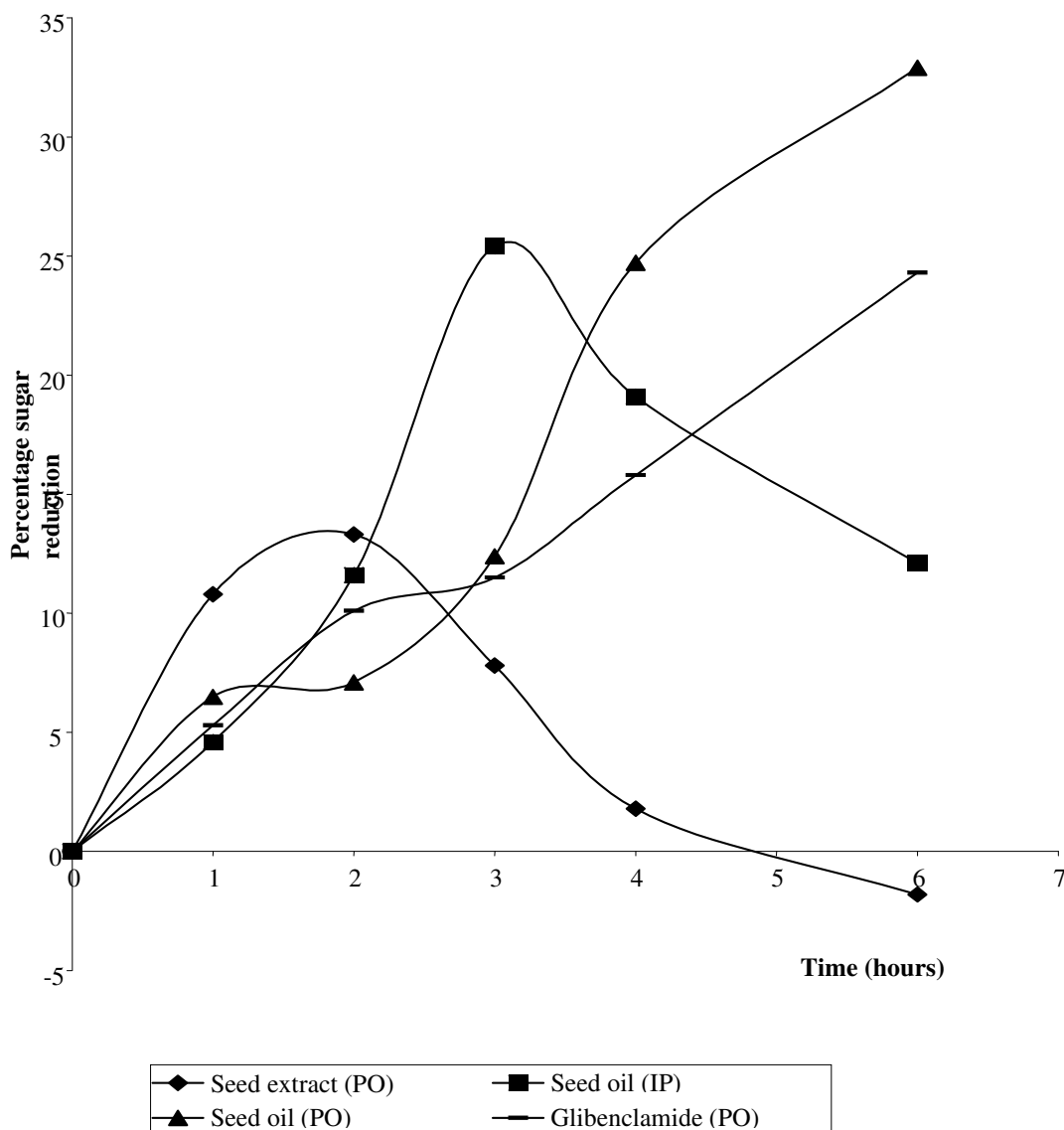
The administration of seed oil IP at 1.0 ml/kg produces an initial increase in blood sugar level. This increase also occurred when the dose level was reduced to 0.25 ml/kg of the oil, but disappeared when the dose level was 0.125 ml/kg. The dose of 0.125 ml/kg gave a consistent blood glucose reduction for three hours with maximum blood glucose reduction of 64.5 mg/dL, representing 25.4 % of the base line. To rule out the presence of hyperglycemic factors in the seed oil, 1.0 ml/kg of normal saline was administered using the same route. This produces an initial increase in blood sugar. However, when the seed oil was given orally at 2 ml/kg, it did not induce initial

hyperglycemic effect as seen with the seed oil given IP. Rather it produces an immediate and sustained hypoglycemic control as can be seen from Figure 1. The increase in blood sugar level after administration of the seed oil IP at 1.0 and 0.25 ml/kg might be attributed to physiological stress. Introduction of foreign bodies into normal animal physiological systems induces some form of physiological stress and stress conditions are well known inducers of certain physiological and biochemical changes in animals including man. [7] It is believed that foreign bodies (e.g., exogenous pyrogens) act on the immune cells particularly mononuclear phagocytes, and may, thereby, induce the production of endogenous pyrogens. [8] The endogenous pyrogens, often known as a group of proinflammatory cytokines, signal the brain through several means to produce or release several biochemicals that lead to observed changes such as fever, increased heart rate, and increased blood pressure. Particularly, stimulation of visceral (vagal) afferent nerves will lead to the release of the neurotransmitter epinephrine. [9] The pharmacological implication of this, including stimulation of  $\beta_2$  receptors in the liver to increase plasma glucose, is well known. [10] The blood sugar reduction effect of the seed oil administered IP at 0.125 ml/kg was compared with the seed oil and seed extract administered PO (Fig. 1). The seed oil was given PO at 2.0 ml/kg while the seed extract was given at 500 mg/kg. The seed oil given PO had a consistent blood sugar reduction that lasted beyond six hours. This is unlike the IP administration. At the sixth hour, the seed oil given PO had a maximum blood sugar reduction of 57 mg/dL representing 32.9 % of the baseline value. The maximum blood glucose reduction of seed extract stood at 72.0 mg/dL representing 13.2 % from the base line blood sugar. This occurred within two hours of administration through oral route. Maximum blood sugar reduction of glibenclamide occurred within 6 hours. The glibenclamide reduced the blood sugar by 57.8 mg d/L representing 24.3 % of the baseline value.

Invariably, it is more beneficial to administer the seed oil through the oral route than through parenteral route because of greater volume that can be tolerated. More importantly, administration of *P. nitida* seed oil is much better than that of seed extract administration. The seed extract effects waned off after 2 hours, but the effect of the seed oil continued well beyond six hours and is higher than the blood sugar control of glibenclamide at 5 %  $\alpha$ - level. This may be attributed to the slow metabolization of the seed oil in the gastrointestinal tract. Further investigation is ongoing to formulate the *P. nitida* saponins (where the hypoglycemic activity has been shown to reside), into a suitable oily vehicle with similar viscosity to that of *P. nitida* seed oil. This will circumvent the poor yield of the seed oil. The saponins can be obtained from any parts of the plant. Such oily formulation may be packaged into soft gels. This will enable the utilization and maximization of the *P. nitida* seed oil based drug through oral route.

**Table 1: Hypoglycemic effect of *P. nitida* seed oil administered parenterally**

Preparation	Dose (ml/kg)	Blood glucose (mg/dL)					
		0 hour	1 hour	2 hours	3 hours	4 hours	6 hours
Seed oil (IP)	1.000	90.0±10.0	94.5±12.9	96.0±8.9	72.8±7.5	70.5±8.0	61.6±7.5
Seed oil (IP)	0.250	72.0±12.2	80.5±2.0	81.0±2.5	69.5±2.9	59.5±5.3	48.5±2.0
Seed oil (IP)	0.125	86.5±4.5	82.5±4.5	76.5±2.0	64.5±1.2	70.0±5.7	76.0±4.1
Normal saline (IP)	1.000	79.0±0.8	94.5±0.4	99.0±4.5	80.5±6.5	84.0±1.6	85.5±5.3
Control	Nil	85.7±2.9	81.0±6.5	86.0±0.8	89.0±1.4	76.0±8.5	79.5±6.9



PO: Oral administration, IP: Intraperitoneal administration.

**Fig 1: Percentage blood sugar reduction Vs time**

**CONCLUSION:**

Administration of the *P. nitida* seed oil through the oral route gives greater blood sugar reduction activity, being 32.9 % compared to the baseline and lasted beyond six hours. The parenteral administration of the seed oil which stood at 25.4 % lasted for three hours. The blood sugar reduction of the seed extract and glibenclamide stood at 13.0 and 24.3 % respectively. The blood sugar reduction activity of the seed extract waned off after two hours, though that of glibenclamide continued well beyond the sixth hour.

However the oral administration of the seed oil gives a blood sugar control than glibenclamide.

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