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Alkaloids of *Cucumis Metuliferus* fruit pulp reduces hepatitis b virus (HBV) in laboratory animals

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Abstract

Objective: Studies on the effects of the alkaloids of *Cucumis metuliferus* fruit pulp on hepatitis B virus was investigated in albino rats.

Materials and Methods: The alkaloids from *C. metuliferus* fruit pulp were isolated according to the method described by Agrawal and Paridhavi [1] and the effect of the isolated alkaloids was assayed in albino rats infected with hepatitis B serum.

Results: Results obtained showed that 50 – 200mg/kg of the alkaloids produced dose – dependent statistically significant ($p < 0.05$) decrease in the levels of serum alkaline phosphatase (ALP), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in albino rats infected with hepatitis B serum.

Conclusions: This result showed that alkaloid isolated from the fruit of *C. metuliferus* plant may have some protective activity against hepatitis B virus (HBV).

Keywords: Hepatitis B virus, alkaloids, *C.metuliferus* fruits, biochemical parameters.

Introduction

Hepatitis can be described as a diffuse inflammatory disease of the liver which may be associated with hepatocellular necrosis affecting the acini, and are caused by different types of viruses including hepatitis B virus [2]. This virus has surface antigens that are labeled HB_sAg, HB_cAg, and HB_eAg [3]. Replication of HBV has been shown to be solely in the liver, perhaps other extra-hepatic replication sites also exist [4].

Studies have shown that treatment of liver disease using orthodox approach has been so difficult, and herbal preparations have been useful for the treatment of liver disorders [5]. The need for the development of an efficient hepatoprotective drug from the natural resource is therefore a necessity [6]. The use of herbs as antiviral agents have been documented scientifically [7]. These authors further stated that alkaloids isolated from these plants have been proven to have antiviral properties. Though, the antiviral properties of the ethanolic crude extract of *C. metuliferus* fruit have been reported [8], not much have been documented on the activities of the alkaloidal content of the plant on hepatitis B virus. The purpose of this study was therefore to investigate the antiviral properties of the alkaloids on hepatitis B virus-induced liver damage of albino rats.

Materials and Methods

Plant Collection and Authentication

The ripe fruit of *C. metuliferus* were harvested from Chong'openg of Jos South Local Government Area of Plateau State, Nigeria. The plant was identified and authenticated by Professor C. O. Akueshi of the department of plant science of the University of Jos, Nigeria.

Preparation of *C. metuliferus*

The mesocarp of the fruits and seeds were carefully scooped out of the pericarp using a spatula and was well stirred after which the yellowish fibrous portion was sun-dried. Sieves of different sizes were used to separate the seeds from the greenish fluidy portion, after which the fluidy portion was spread on trays and placed in an oven set at 55 °C until it was dried. The yellowish and the greenish dried portions were then mixed and reduced to fine particle size using mortar and pestle.

Isolation of Alkaloids of the *C. metuliferus* Fruit Pulp

The alkaloids from *C. metuliferus* fruit pulp were isolated according to the method described by Agrawal and Paridhavi [1]. The pure alkaloid was stored in an air-tight container at room temperature prior to use.

Ethical Clearance

Ethical clearance on the proper handling and use of animals and their products was obtained from the ethical Committee on Animal use of the Department of Pharmacology and Toxicology, University of Jos, Nigeria.

Effect of Alkaloids Isolated from *C. metuliferus* Fruit Pulp on Hepatitis B Virus-Induced Liver Damage

Twenty five adult albino rats (wistar strain) were divided into five groups of five animals each. Animals in group 1 (control group) were administered equi-volume (per kg body weight) of normal saline. Animals in group 2 were administered 0.2ml/kg of hepatitis B virus serum. Those in group 3, 4, and 5 were respectively pretreated with 0.2ml/kg of hepatitis B virus serum ip, 3hours daily before they were treated with 50,

100 and 200mg/kg of the *C. metuliferus* alkaloids orally using orogastric tube daily for a period of 14 days^[9]. After twenty four (24) hours of the last administration, the animals were made unconscious using petroleum ether, and blood samples were collected through cardiac puncture for biochemical studies.

Statistical Analysis

The results were presented in mean±SEM, and the levels of significance were carried out using two-way ANOVA and student *t-test*, and a probability value of $P<0.05$ was considered statistically significant.

Results and Discussion

Table I: Effect of the alkaloids of *C. metuliferus* fruit on hepatitis B virus – induced hepatotoxicity in albino rats

Treatment (Mg/kg)	Total protein (g/L)	Albumin (g/L)	ALP (u/L)	ALT (u/L)	AST (u/L)
Normal saline	72.25±2.53	27.50±1.60	345.75±42.29	12.20±1.93	55.00±5.61
HBV serum	73.25±3.12	29.10±1.78	407.25±20.25	18.50±3.50	66.50±6.33
HBV + 50 alkaloids	78.25±3.35	30.25±0.63	212.50±44.17*	14.00±1.15*	61.25±4.50
HBV + 100 alkaloids	71.50±1.55	27.75±1.89	182.25±3.81*	10.00±2.50*	61.75±2.50
HBV + 200 alkaloids	75.50±4.09	31.75±0.75	131.50±18.73*	12.50±2.84*	5.25±15.63*

n = 5, * $P<0.05$

The results on the effect of the alkaloids of *C. metuliferus* fruit on the biochemical parameters of hepatitis B virus – induced liver damage showed significant ($P<0.05$) dose-dependent decrease in the levels of alkaline phosphatase (ALP) and alanine aminotransferase (ALT) compare to the control group (Table 1). The decrease in the levels of aspartate aminotransferase (AST) was also statistically significant ($P<0.05$) in the group treated with 200mg/kg of the alkaloids.

Previous studies have shown that changes in serum enzymes concentration may be a signal of hepatic pathological process^[10, 11]. It has been reported that both ALT and AST are located in the cytoplasm and mitochondria of liver cells, and also in cells of the heart, skeletal muscles, kidney and brain^[12]. These authors further stated that the activities of ALT outside the liver are low and hence this is considered more specific for hepatocellular damage. ALP has been reported to be widely distributed in the body with significant activities in the liver, gastrointestinal tract, bone marrow and placenta^[12, 13]. Studies have shown that the mechanism underlying drug and chemically induced hepatotoxicity is free radicals activities through lipid peroxidation and oxidative stress^[14]. The observed dosed – dependent decrease in the levels of enzymes concentrations is suggestive of the protective effect of the administered alkaloids in the animals, which could be by antioxidation through the process of mopping up or scavenging of free radicals generated during hepatic injury^[15, 16].

Conclusions

This study has revealed that alkaloids isolated from *C. metuliferus* fruit have some activities against hepatitis B virus (HBV). Further studies need to be carried out to ascertain the type of alkaloid(s) responsible for such properties and its mechanism of actions.

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