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GASTRIC ACID SECRETION, MUCUS CONCENTRATION AND ULCERATION FOLLOWING OROGASTIC FEEDING OF CANNABIS SATIVA TO ALBINO WISTAR RATS

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ABSTRACT

This study was carried out to evaluate the effect of consumption (ingestion) of *Cannabis sativa* on the gastrointestinal tract using mucus concentration, acid secretion and ulceration in animal (rats) model as indices. Three groups of six (6) rats each were used. The control group were fed on rat chow only while another group were fed on low dose of *Cannabis sativa* 0.5gm/100g body weight and another group were fed on high dose of *Cannibis sativa* 0.8mg/100g body weight for 28 days respectively and allowed free access to food and water. At the end of 28 days, the results showed that the acid secretion in the high dose group was significantly ($P<0.001$) higher than in low dose group while the mucus concentration in low dose and high dose group respectively were significantly lower ($P<0.01$) than control. The mucus concentration in high dose was significantly lower ($P<0.001$) than low dose group when the test groups were compared. Similarly the ulcer scores were higher in low dose group ($P<0.05$) and in high dose group ($P<0.001$) respectively when compared with control group. The ulceration in high dose group was significantly higher ($P<0.001$) than the low dose group. In conclusion, ingestion of *Cannabis sativa* causes decrease in adherent gastric mucus, increase acid secretion and increase in gastric ulceration in a dose dependent fashion. The liberal use of *Cannabis sativa* should therefore be discouraged.

KEYWORDS: Gastric acid, mucus, ulceration, *Cannabis sativa*

INTRODUCTION

Cannabis sativa is a dioecious annual green and leafy plant. It is well adapted to temperate climate. The most important cannabis sativa products in food and drug trade are whole hemp seed, hulled hemp seed, hemp seed oil, marijuana and hashish (Adams and Martin, 1996).

Herbal cannabis contains over 400 compounds including 60 cannabinoids which are aryl substituted meroterpenes. The most potent ingredient is Delta-9-tetrahydrocannabunol (THC) (Pillard, 1970).

Hemp is increasingly spoken of as one of the nutritionally complete food sources in the world, second only to soyabeans (Amerio, 1998; Callaway, 2004). Hemp protein contains amino acids considered a high quality and highly digestible protein source. It also contains Omega 3 and Omega 6 fatty acids which are good for the body system (Osborne and Curtis, 2007).

The route of administration is mostly smoking where about 50% of the THC is inhaled in the main stream smoke and absorbed in the lungs from where it gets to the brain (Maykut, 1985). An alternative route of administration is by ingestion as tea, food additives, as active ingredients in drugs, salad dressing and vegetable juices (Ontario Hemp alliance Hemp Information. <http://www.Ontariohempalliance. org/info/pinfo.cfm). The bioavailability of cannabis

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sativa after oral ingestion is low and the duration prolonged because of slow absorption from the gut, (Maykut, 1985; Besett, 2008).

Cannabinoids are lipid soluble and have been found to be of medicinal importance where it is used to relieve nausea, muscle spasm and analgesia (Hemp and Cannabis Foundation, 2009). It combines the properties of alcohol, tranquilizers opiates and hallucinogens (Sameth, 2007). Chronic consumption of cannabis sativa has been found to cause infertility in both males and females (Graham, 1998; Hall and Solowij, 1998) psychotic reactions (Johns, 2001), loss of memory and impaired psychomotor coordination (Tommy *et al,* 2008).

It has been documented to cause decrease salivary flow from maxillary gland leaving dry mouth (Prestiffilipo *et al*, 2006) and antagonise the action of both endogenous and exogenous insulin (Nakata and Yada, 2007).

Work on clinical studies with cannabinoids on the gastrointestinal tract is very scanty even though Pertwee, (2001) has document his findings on the acid secretion in human. No elaborate work has been done to determine the effects on other factors that culminate to gastric ulcers. This work was therefore undertaken to study how ingestion of *Cannabis sativa* affects acid secretion, mucus concentration and ulceration among cannabis users.

2. MATERIALS AND METHODS

2.1. COLLECTION AND PREPARATION OF EXTRACT

Cannabis sativa was obtained from a farm in Calabar South Local Government Area of Cross River State, Nigeria. It was certified and classified by botanists of the University of Calabar Botanical garden. The cannabis was dried in an oven and blended into snuff-like particles and weighed. The particles were then soaked in 1000mls of water for 12 hours and then filtered using Whatman's No. 1 filter paper. The filtrate obtained was dried using Astell Hearson oven at 45°C and the dry extract collected and kept in an airtight container and weighed.

2.1.1. PREPARATION OF *CANNABIS SATIVA* AND ADMINISTRATION

One gram (1g) of the extract was dissolved in 100mls distilled water. After the LD_{50} was obtained, the low dose (LD) was taken as 0.5mg/100g body weight and high dose as 0.8mg/100g body weight. The rats were divided into three groups of 6 rats each. The groups are control, low dose group and high dose group. All the three groups were allowed free access to water and food and in addition the low dose and the high dose group were administered orally on daily basis low and high doses of *Cannabis sativa.* The oral administration of the Cannabis was by using an oropharyngeal cannula and the feeding lasted for 28 days.

2.3. COLLECTION OF GASTRIC ACID

Gastric acid collection was by the method of Gosh and Schild (1958). The rats were fasted overnight prior to the experiment. The rats were anaesthetized with urethane 0.6ml/100g body weight intraperitoneally). An incision was made along the linea alba after insertion of a tracheal cannula. The effluent was obtained from the stomach using normal saline. Histamine, (0.3mg/kg body weight) was administered subcutaneously and later cimetidine (0.2mg/kg body weight) intramuscularly were administered to determine their effects on acid output.

2.3.1. MUCUS EXTRACTION

The adherent mucus was extracted by the method of Okwari, (1999). The stomach was removed and washed in normal saline and opened along the greater curvature and mounted on a corkboard. Mucus was extracted from the stomach using a spatula into a beaker of known weight having 4mls of water. The weight of the mucus was then taken as final (beaker, $+H_2O$ + mucus) weight of beaker minus initial weight (water + beaker only).

2.3.2. DETERMINATION OF GASTRIC ULCERATION

Ulcers were induced by the use of acid/alcohol method. After opening and occluding the stomach, an orogastric cannula was used to instil 1.5ml of acid alcohol preparation (equivalent of 0.1N HCl and 70% ethanol) and left for 1 hr. The stomachs were harvested and incision made along the greater curvature to expose the mucosa wall. Scoring of ulcer spots was done by the method of Alpin and Ward, (1967) as used by Adeniyi and Oluwole, (1990).

Ulcer scores were graded thus;

Grade	Interpretation
0.0	No lesions (Normal stomach)
0.5	Pin size ulcer
1.0	2mm or more haemorrhagic or small linea ulcer
1.5	Ulcer spot greater than 3mm

2.4. STATISTICAL ANALYSIS

Results were presented as mean ± standard error of mean. Statistical significance between the groups were analysed by means of students t-test and Anova, followed by a post hoc least significant difference (LSD) test using SPSS version 15.0 for windows. P value less than 0.05 were considered statistically significant.

3.0. RESULTS

3.1. GASTRIC ACID SECRETION

The mean basal gastric secretion in the control, low dose and high dose of C. sativa are as shown in Fig. 1.

The result shows that there was significant increase (P<0.001) in basal acid secretion in low dose and high dose group respectively when compared with control. Between the low dose and high dose group, the basal acid secretion was significantly higher (P<0.001) in high dose group when compared with low dose. After the administration of histamine, the peak acid secretion in low dose became significantly higher (P<0.001) than high dose and control group respectively. The addition of cimetidine an H_2 blocker and an antagonist of histamine greatly reduced acid secretion in all three groups studied. In comparison, the acid secretion in high dose group after administration of cimetidine was significantly (P<0.001) higher than that for low dose and control group (P < 0.01) respectively.

3.2. MUCUS CONCENTRATION

The mean mucus concentration in control, low dose and high groups are as shown in Fig 2. The mucus concentration in low and high dose group were each significantly lower (P<0.01) than control. The mucus concentration in high dose group was significantly lower (P<0.001) than in low dose. This represented about 7.19% increase from control to low dose, and 49% increase from low dose to high dose of *Cannabis sativa*.

3.3. GASTRIC ULCERATION

The ulcer score increased from the control value of 7.6±0.23 to 9.7± 0.32 and 13.4±0.48 in the low and high dose groups respectively. This represented 21.65% increase in ulceration from control to low dose group and 27.4% increase from low dose to high dose group. This is as shown in Fig. 3.

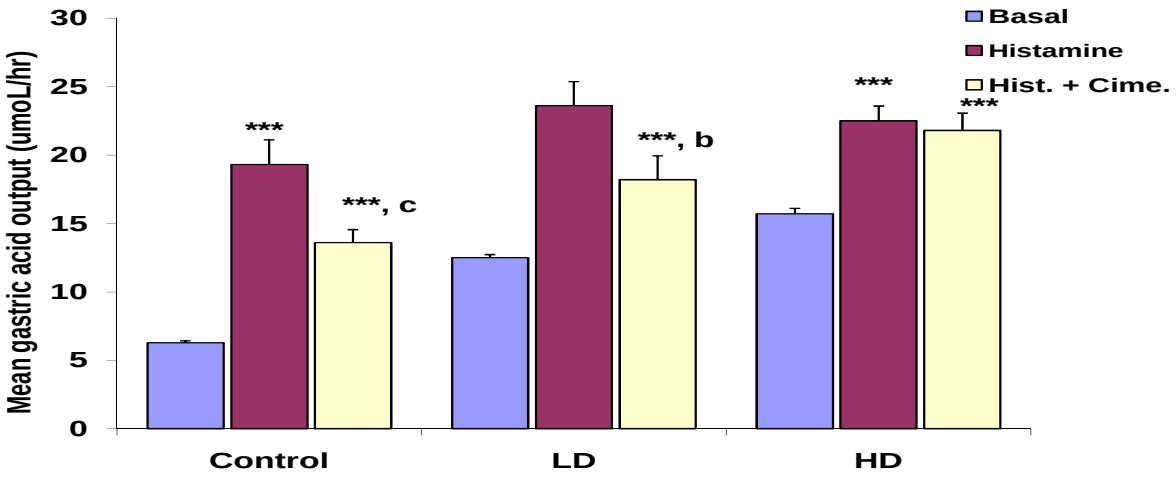

FIG. 1 Effect of histamine and cimetidine on gastric acid output in the different experimental groups. Values are mean ± SEM, n = 6.
*****P<0.001 vs control; b = P<0.01, c = P<0.001 vs LD.**

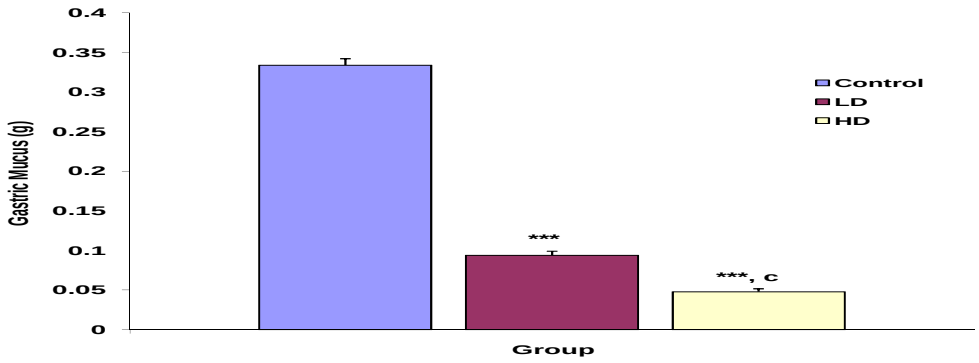

Fig. 2 Comparison of mucus secretion in the different experimantal groups. values are mean ± SEM, n = 6. **P<0.01 vs control; c = P<0.001 vs LD.

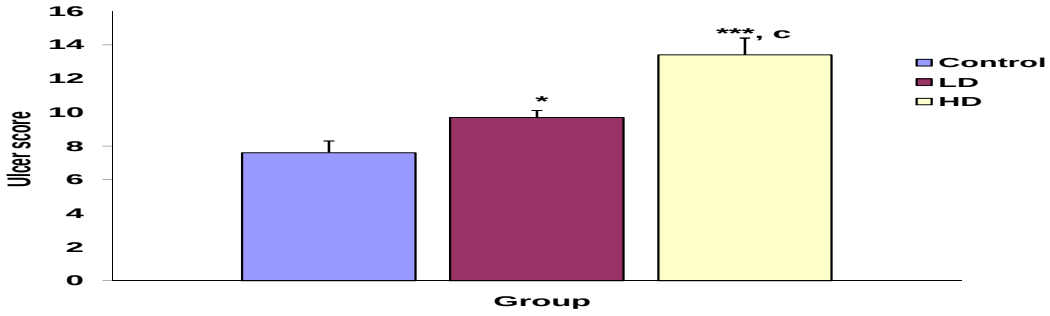

Fig. 3 Comparison of ulcer scores in the different experimantal groups. values are mean ± SEM, n = 6. *P<0.05, ***P<0.001 vs control; c = P<0.001 vs LD.

DISCUSSION

The effect of ingestion of *Cannabis sativa* at low and high doses for 28 days on gastric acid secretion, mucus concentration and ulceration was studied. The results show that chronic ingestion of *Cannabis sativa* leads to increase in gastric acid secretion and gastric ulceration respectively and a decrease in mucus secretion. The increase in ulceration was probably as a result of the increased acid secretion and decreased mucus concentration. Adherent mucus appears to help reduce the effect of gastric acid secretion on the gastric mucosa and any reduction in the mucus exposes the mucosa to acid degradation.

The results are contrary to the finding of so many reporters. Germano *et al*, (2001); Adami *et al,* (2002) found that cannabinoids a major component in cannabis reduces gastric acid secretion and even protects the gastrointestinal tract against stress induced ulcers. The inhibitory action has been attributed to receptors localized in vagal nerves terminals innervating the external gastric (Pillard, 1970). Cannabis has been documented to be very useful in the treatment of nausea and stimulation of appetite (Mckim, 2002). Moor and McQuay, (2005) have a contrary opinion as they found out that chronic consumption of cannabis has systemic effects on users which confirms that individual differences and adverse events result from its use and this include nausea, dry mouth and constipation (Prestiffilipo *et al*, 2006).

The difference in our findings may likely be due to the specie of cannabis used as well as duration of use. It has been documented that the effect of cannabis can vary greatly depending on which sub-specie or strain one medicates with or uses. While the indica strain which is mostly reported has sedative/relaxant effect with a higher level of cannabinoids, the sativa, a sub-specie used in this study contains less cannabinoids and is more of a stimulant with a higher level of tetrahydrocannabinoid (THC) (http/www marijuana seed. net. 2012). Besides this, the different environments where the cannabis is grown influences the chemical content as well as hereditary determinants (Pate, 1994; Kirkham, 2006).

Corruzzi et al (2001) have reported that even though cannabis is widely reported to decrease acid secretion, this is only true for histamine induced secretion but not for basal secretion. The difference in the specie of cannabis used may have contributed greatly to our results.

In conclusion, chronic ingestion of *Cannabis sativa* may lead to increased gastric acid secretion, decreased adherent mucus and increased ulceration in rats. The liberal use of *Cannabis sativa* should be discouraged.

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