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Comparative Studies of the Treatment of Nicotine and Tobacco on Cytoprotection of Gastrointestinal Tract Using Albino Wistar Rat

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ABSTRACT- The effect of Nicotine and Tobacco on cytoprotection in albino Wistar rats were studied. Total 18 albino Wistar rats were randomly assigned to three groups of 6 rats each. Group I rats were given normal rat feed and water to serve as a control, while group II rats were fed with tobacco diets and group III rats were fed with nicotine diet and water, for 28 days respectively. After 28 days, the animals were starved for 16 hours. After which they were anesthetized with 6ml/kg of 25% of v/v solution of Urethane. The stomach of the animals was isolated, washed and rinsed with normal saline for ulcer study. The total ulcer scores in rats fed with nicotine diet were significantly higher ($p<0.05$) compared to control the same trend of result as in the total ulcer score were obtained in grade 2.0 ulcer in rats fed control, nicotine and tobacco diet the result suggested that refined nicotine and nicotine present in tobacco can suppress the cytoprotection of the gastrointestinal mucosa and hence ulceration of the gastrointestinal mucosa.

Key-Words- Cytoprotection, Nicotine, Tobacco, Wistar rats, Gastrointestinal tract

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INTRODUCTION

Tobacco belongs to the genus Nicotiana, which is named from Jean Nicot, the then French ambassador to Portugal (Macon 1994). There are many species of tobacco but tabacum and rustica are the two common one (Hecht, 1989). Tobacco is used in two major forms: the smokers and the smokeless. The smokeless tobacco has different nature names according to Thomsen (2008), these are: Ntsu in South Africa, Toombak in Sudan, Shammah in South Arabia, plug chew in the United States.

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In Nigeria, the common names are Anwuru in Igbo, Taba in Yoruba and Hausa languages. Anxiety is the normal emotional and physiological response to feeling threatened. Different people behave differently when threatened. They may either run or fight however there are some threats that beforehand determine whether it will be flight or fight (Jorge, 2000).

Exposure to tobacco nicotine either from cigarettes and other forms of tobacco including cigars, pipe tobacco, snuff, and chewing tobacco has been reported to be associated with alteration in the normal functions of the brain and the whole nervous system (NIDA, 2009a; Charles, 2000; Katzung, 2005 and NIDA, 2009b) Nicotine is used to aid smoking cessation and other nicotine addictions (Charles, 2000; Katzung, 2005). Using a controlled amount of nicotine helps to reduce nicotine withdrawal symptoms when one attempts to quit the use of

tobacco products (NIDA, 2009b; Charles, 2000; Adeniyi, 2007).

Nicotine is highly addictive. People who regularly consume nicotine and then suddenly stop experience withdrawal symptoms, which may include cravings, a sense of emptiness, anxiety, depression, moodiness, irritability, and inattentiveness. The American Heart Association says that nicotine (from smoking tobacco) is one of the hardest substances to quit at least as hard as heroin. According to a report published by the Massachusetts Dept of Public Health, tobacco companies steadily increased the nicotine content of their cigarettes from 1998 to 2004, by approximately 10%. The higher the nicotine dose in each cigarette, the harder it is for the regular smoker to quit. The Department accused the tobacco companies of deliberately making their customers more addicted, so that they could secure sales. Doctors complain that this business strategy of getting customers more hooked undermines the success rates of smoking cessation therapies. (Medical News today, 2012) nicotine is also an anti-herbivore chemical, specifically for the elimination of insects.

When humans, mammals and most other types of animals are exposed to nicotine, it increases their heart rate, heart muscle oxygen consumption rate, and heart stroke volume. The consumption of nicotine is also linked to raised alertness, euphoria, and a sensation of being relaxed. Nicotine at low doses directly stimulates the CNS especially the brainstem resulting in sympathetic neural discharge, which increases blood pressure and heart rate among other behavioural stimulations (Comroe 1960; Su 1982).

According to Wu and Cho (2004) increase use of tobacco and its related health problems are a great concern in the world. Recent epidemiological findings have demonstrated the positive association between cigarette smoking and several gastrointestinal (GI) diseases, including peptic ulcer and cancers. Interestingly, smoking also modifies the disease course of ulcerative colitis (UC). Nicotine, a major component of cigarette smoke, seems to mediate some of the actions of cigarette smoking on the pathogenesis of GI disorders. Nicotine worsens the detrimental effects of aggressive factors and attenuates the protective actions of defensive factors in the processes of development and repair of gastric ulceration.

Nicotine also takes part in the initiation and promotion of carcinogenesis in the GI tract. In this regard, nicotine and its metabolites are found to be mutagenic and have the ability to modulate cell proliferation, apoptosis, and angiogenesis during tumoriogenesis through specific receptors and signaling pathways. However, to elucidate this complex pathogenic mechanism, further study at the molecular level is warranted. In contrast, findings of clinical trials give promising results on the use of nicotine as an adjuvant therapy for UC. The beneficial effect of nicotine on UC seems to be mediated through multiple mechanisms. More clinical studies are needed to establish the therapeutic value of nicotine in this disease (Wu and Cho, 2004).

Mucus and other secretions line the gastrointestinal tract, protecting it from gastric acid. If this protective mechanism is impaired or if there is an increase in gastric acid or other damaging agents, then ulceration may occur. Peptic ulcer disease involves the formation of ulcers in either the lining of the stomach (gastric ulcers) or the duodenum, the section of the small intestine closest to the stomach (duodenal ulcers).

The presence of the gastric bacterium *Helicobacter pylori* causes infection and damage to the gastrointestinal wall, greatly increasing the risk of developing peptic ulcers. The *Helicobacter pylori* organism is present in all people with duodenal ulcers and 70–90% of people with gastric ulcers. The risk of developing peptic ulcers is also increased among people who take non-steroidal anti-inflammatory drugs (NSAIDS).

Peptic ulcers were the eleventh most common cause of hospital admissions in Australia in 2007–2008, (Australian Institute of Health and Welfare, 2010) and almost 3% of Australians report having some sort of peptic ulcer (Australian Institute of Health and Welfare, 2004).

Smoking increases the risk of peptic ulcer disease in people who are infected with *Helicobacter pylori*. In Australia, about 9% of peptic ulcer disease in men and 6% in women have been attributed to smoking (Ridolfo and Stevenson 2001).

Smoking affects the gastrointestinal tract in a number of ways: it reduces the production of gastric mucus and other protective secretions, promotes duodenal reflux and reduces blood flow to the lining of the tract. In this compromised environment, *Helicobacter pylori* are better able to spread and cause damage. Smoking may also be related to an increased risk of developing complications of peptic ulcer disease, such as ulcer perforation or bleeding, but this effect may be confined to people who are not taking NSAIDS.(US Department of Health and Human Services, 2004).The increased risk of peptic ulcer disease consequential to smoking appears to reverse with smoking cessation.

MATERIALS AND METHOD

Experimental animals

Randomized selection of eighteen (18) albino Wistar rats into 3 groups of 6 rats each was done.The groups were labeled group I, II and III. Group I served as the control group and were fed with normal rat chow, while groups II and III were the experimental groups fed with tobacco and nicotine diet respectively.

Before the experiment, the animals were kept in the animal house of the Department of Physiology, University of Calabar in well ventilated capes under normal feed ration for acclimatization. Animals were then divided into groups as mentioned earlier and were left to acclimatize for a period of 14 days.

Preparation of extracts and animal feed

Tobacco leaves were acquired from Ugep in Yakurr Local Government Area of Cross River State. The leaves were washed and sun dried for 7 days to ensure proper dryness, after which they were placed in an Ausreu Hear-son microwave oven at a temperature of 40-50^{0}C in the department of physiology, University of Calabar, until the leaves were crispy and easy to blend. The leaves were then grounded to fine powder.

100g of rat chow was mixed with 2g of the powdered tobacco according to pay 100-2002; to form tobacco diet. This was given to the rats in group II throughout the period of the experiment.

Also nicotine was mixed with 2g of animal chow and this wasted the rats in group III throughout the experiment period.

Astric ulceration method

The animals were starved for 16 hours under anesthesia (6 ml/kg of 25% v/v solution of urethane), a pyloric incision was made and a cannula inserted and kept in place with a thread. The stomach of the animal was instilled with 1.5mls of acid alcohol, prepared from equivolume of O. IN Hcl and 70% ethanol. The instillation was done through the pyloric incision. This was switewed with thread and the animal was left to stay for an hour. The stomach was then isolated, washed and cut open along the greater curvature and rinsed with normal saline. Pins were used to fasten the tissue in place for proper visualization. A magnifying lens and a venire caliper were used to measure the extent of ulceration. Scoring of ulcer spots was by the method of Adeny and Olowokown (1990). Ulcer score was done according to the grading system below.

Table 1: Ulcer score grading system

Grade	Interpretation
0.0	No leision normal stomach
0.5	Pin size ulcer
1.0	2, or more haemahapic or small linear ulcer
2.0	Ulcer sports greater than 3mm

Statistical analysis

Data obtained from the study were analyzed using the students T test. Result were presented as means= standard error of the mean (Sem). Probability level $p<0.05$ was accepted as significant level.

RESULT

Fig. 1 compares total ulcer scores in the control, tobacco and nicotine fed experimental species. Total ulcer scores were seen to be higher in the nicotine fed group relative to the tobacco ($p<0.001$) and control experimental species ($p<0.001$). The ulcer score for the tobacco fed group was significantly lower ($p<0.05$) compared to control.

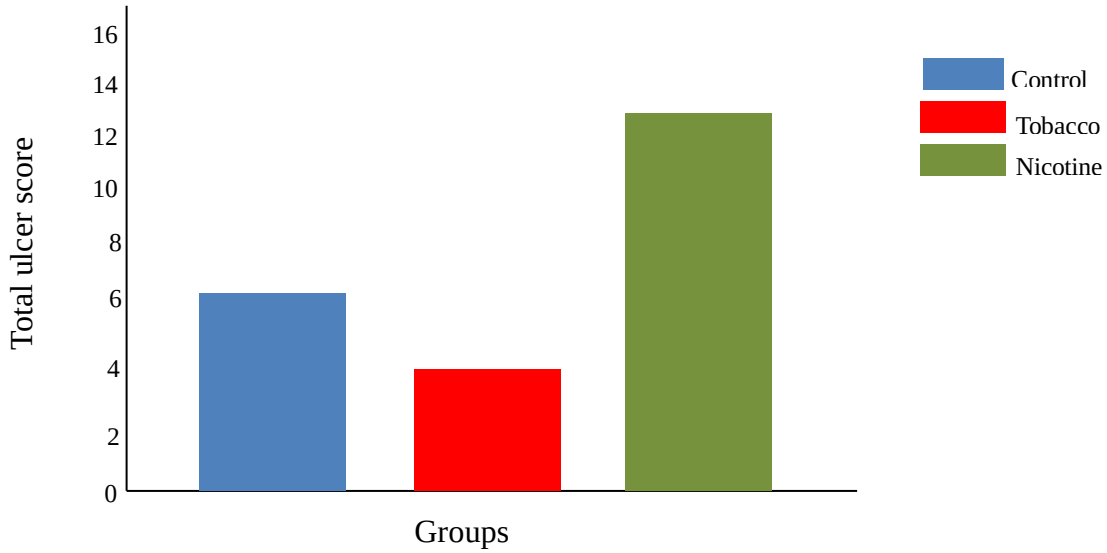
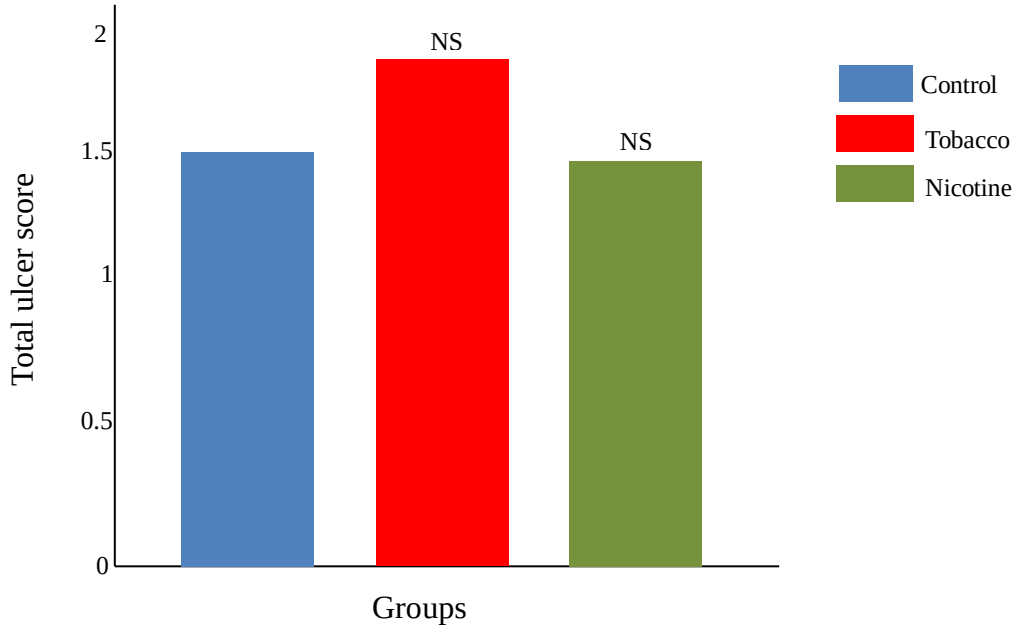


Fig. 1: Comparison between total ulcer scores in rats fed with tobacco, nicotine and control diets

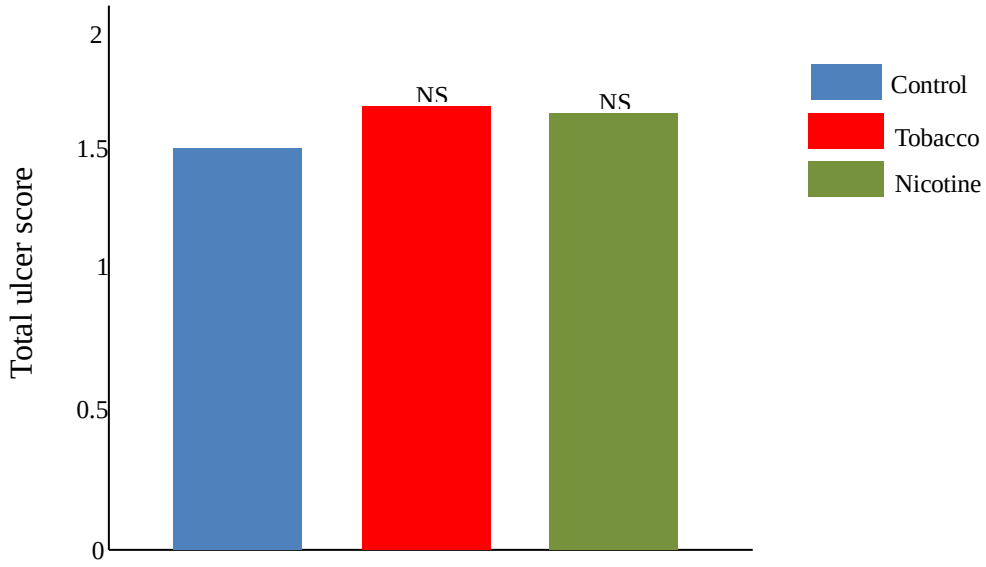
Fig. 2 Shows grade 0.5 ulcer score in the control, tobacco and nicotine fed experimental species. No significant 0.5 ulcer grade score in the tobacco and nicotine groups compared to the control group.



NS = Not significant compared to control

Fig. 2: Comparison between grade 0.5 ulcer scores in rats fed tobacco, nicotine and control diets

Fig. 3 is a comparison of grade 1.0 ulcer scores in the control, tobacco and nicotine group(s) of experimental species. No significant difference between control group and the tobacco and nicotine group(s).



NS = Not significant compared to control

Fig. 3: Comparison between grade 1.0 ulcer scores in rats fed tobacco, nicotine and control diets

Fig. 4 shows grade 2.0 ulcer scores in the three experimental group(s)Grade 2.0 ulcer scores in rats fed nicotine was significantly higher ($p<0.01$) compared to tobacco, and ($p<0.01$) compared to control. The ulcers scores of the tobacco group was however significantly lower ($p<0.01$) compared to control.

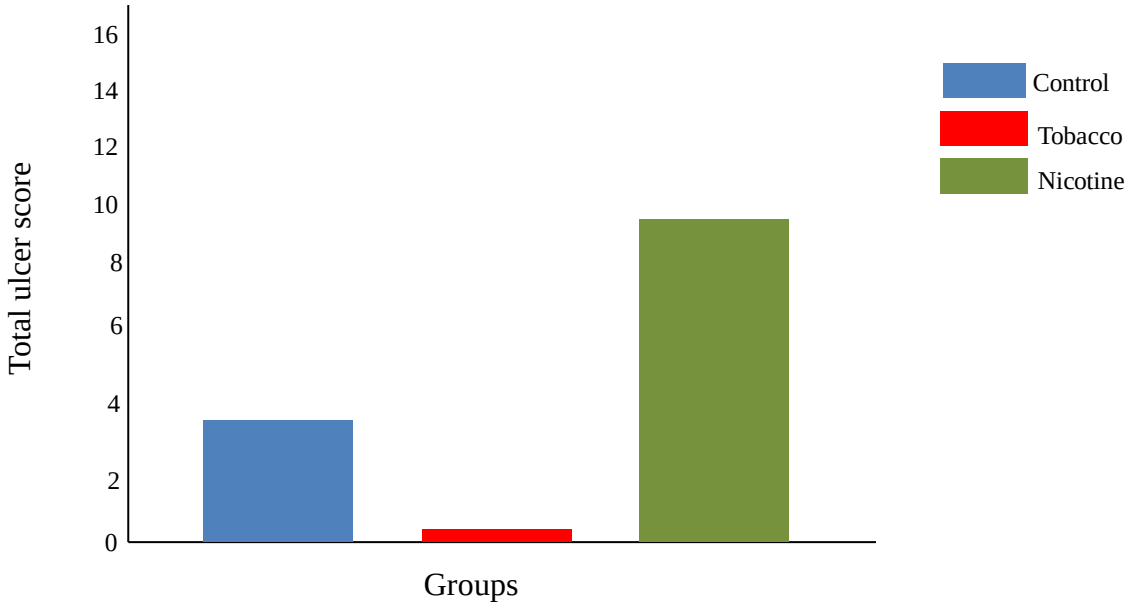


Fig. 4: Comparison between 2.0 ulcer scores in rats fed with tobacco, nicotine and control diets

DISCUSSION

The cytoprotective effect of tobacco and synthetic or purified nicotine was investigated. From the result, it is obvious that oral consumption of nicotine may present damage to the mucosal lining of the gastro intestinal tract. More so, the severity of the damage observed has a positive correlation with the concentration as much as the duration of consumption of nicotine.

Again it can be deduced that the ulceration observed in the experimental species fed with tobacco only is most likely influence by the high concentration of other potent substances in tobacco.

The proceeding argument is justified by the significantly higher total ulcer scores in the experimental group (nicotine fed Wister rats) compared to that of the control group for the same length of time. While the mechanism through which nicotine in tobacco and synthetic nicotine work to produce their effect via same mechanism.

Furthermore, the slow metabolism and clearance of nicotine from the body prolong it effect on gastric acid secretion, which put the G.I.T mucosa at the risk of damage. Interestingly they has been clinical studies detailing high frequency of peptic ulcer in regular and chain smokers (King 1929) although this is beyond the scope of this study can be extrapolated to the human population including persons who orally consume tobacco or nicotine in its synthetic form.

CONCLUSIONS

The results suggest that refined nicotine and nicotine present in tobacco may suppress the cytoprotection of the GIT mucosa and hence may lead to ulceration of the gastro-intestinal mucosa.

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