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HISTOPATHOLOGICAL CHANGES IN STOMACH OF MALE MICE DURING ADJUVANT THERAPY WITH VARIED DOSES OF GENE VAC B VACCINE AND IMMUNEX DS

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ABSTRACT

Modern medical science bounces with a rapid emerging adjuvant therapies these days to combat with life threatening disorders where a specified vaccine coupled with an immunostimulant is administered which heightens the host's immune status. The present study focuses on the utilization of adjuvant therapy in male mice which were induced with varied doses of Gene Vac B vaccine (HbsAg) coupled with a novel, commercially available immunostimulant Immunex DS (IDS). The tissues of stomach were processed for the histopathological changes. The results clearly portray denaturation of cellular constituents and certain damage in the integrity of these tissues. These results indicate the disturbance brought forwarded by IDS when coupled with commercially available Gene Vac B vaccine.

Key Words: Gene Vac B vaccine, Immunex DS (IDS), Stomach, Hepatitis B.

INTRODUCTION

Hepatitis B is caused by HBV virus leading to liver inflammation, cirrhosis and eventually ends up in hepatocellular carcinoma. Hepatitis B causes 1.2 million deaths annually (Nakamoto et al ., 1998). Hepatitis B in acute phase causes morbid and deleterious ailments initiated by general ill health , sudden loss of hunger (Aphagia) , inflammation of the soft joints and ligaments , cystic duct abduction , heavy raise in oxidative stress , renal obstruction facilitated by Membranous glomerulo nephritis (Zhang *et al.*, 2010 ; Fabrizi *et al.,* 2010) , nausea, vomiting, tiredness, severe asthenia, and progress to severe jaundice. The chronic phase is manifested by heavy inflammation of liver, cirrhosis , fat impregnation on the surface of liver, increase in transaminases and lactate dehydrogenase (LDH) levels , increased liver Superoxide dismutase activity (Mary Chatterjee and Sil , 2006) and culminated by Hepato cellular carcinoma (Wong and Goh, 2006). Persons who do not recover from HBV infection became chronic potential carriers'. Now a day s a great deal of research is unveiling in the form of adjuvant therapy where a specified vaccine is coupled with a potentiate immunostimulory drug/product to annihilate this global menace. Immunostimulants can be administered before, with or after vaccine therapy to amply the specific immune response. There are prophylactic or promotive agents acting as immuno-potentiators as well as immuno-therapeutic agents. Immunostimulants are utilized as adaptogenic drugs because of their

fewer side effects and high virtuosity and function.

Such a novel commercial immunostimulant is manufactured by PVS Labs, Andhra Pradesh, India known as Immunex DS (IDS). The profounding impact of IDS lies within its unique formulation which provides a multidimensional effect on the host physiological and immunological status. IDS is a complete and unique amalgamation of many naturally occurring immune-enhances such as beta carotenes, L-lysine, Dl-methionine, essential fatty acids, Livamisol hydrochloride , Vitamins (A, D_3, E. C and B_{12}), minerals (Zinc, cobalt , manganese, and Selenium) and probiotics. IDS improve and enhance the strength, vigor and vitality of the host. It provides a positive effect on the growth of the host. It is constructive to stimulate body's defense mechanism yielding an increased immune response. It also relieves the stress. IDS prevent the colonization of the harmful bacteria in the gastro-intestinal tract. The focal theme of this study is the implementation of IDS in male Swiss albino mice (*Mus musculus albinus*), which were triggered by a burning prodigy of human health scenario, that is, Hepatitis B and challenge its immunocompetence in the light of histopathological studies in gastro-intestinal tract of mice.

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MATERIALS AND METHODS

Male Swiss albino mice (*Mus musculus albinus*) (6-8 weeks of age, Average weight 23-31g) were used in the present investigations According to the guide lines of CPCSEA (Committee for the purpose of control and supervision of experiments in animals), proper acclimatization was maintained. Eight groups of mice were maintained 10 in each group. Six groups of mice(A, B, C, D, E and F) were orally intubated with 150mg of IDS with the help of a syringe fitted with a 3 inch 16gauze oral, blunt feeding needle. Later these six groups of mice were inoculated with various doses of Gene Vac B HbsAg vaccine intramuscularly. One group of mice (c) were intubated orally by giving 150mg of IDS and served as immunostimulated control and another group (cc) of mice was neither intubated with IDS nor inoculated served as normal controls for comparison. The mice (groups A, B ,C, D, E and F) were immunostimulated on day 0 and inoculated with different doses of Gen Vac B HbsAg vaccine on day 7 and waited for 72 hrs, later from day 11 to 15 the mice were sacrificed along with the mice of Immunex DS treated alone (group c) and normal ones (group cc). Tissues of stomach were taken, were fixed, sectioned (5µm) and stained for H&E method for histopathological studies

RESULTS

All the experimental mice pertaining to groups A , B, C, D , E and F survived along with IDS treated alone mice (group c) and normal controls (group cc) . The immunostimulated and vaccinated mice (experimental mice) showed signs of acute illness , anorexia , heavy darkish rough textured tumors along the cervical region. Pale enlarged liver with sumptuous fatty depositions were noticed in mice of groups (D ,E and F). The experimental mice which were treated with high doses of vaccine (groups E and F) vividly manifested highly inflamed and ulcerative gastro-intestinal tract. The stomach and large intestine of these mice turned yellowish in color due to excessive accumulation of bile in it due to impaired liver and cystic duct function. This clinical finding clearly gives an insight of gastritis and enteritis in severe hepatitis B condition.

Histopathological Findings in Stomach:

T.S of stomach of mice treated with IDS : the T.S of stomach of IDS treated animals (group c) showed clear and healthy serosa , Longitudinal muscle layer , circular muscle layer , sub mucosa , longitudinal layer of muscularis mucosa , circular muscle layer of muscularis mucosa and gastric folds.

Day 11: The gastric folds showed normal texture, and the mucosal lining of gastric folds are clear and normal. The secretary sheath of the glandular epithelium is intact. No marked changes were observed in the stomach of mice

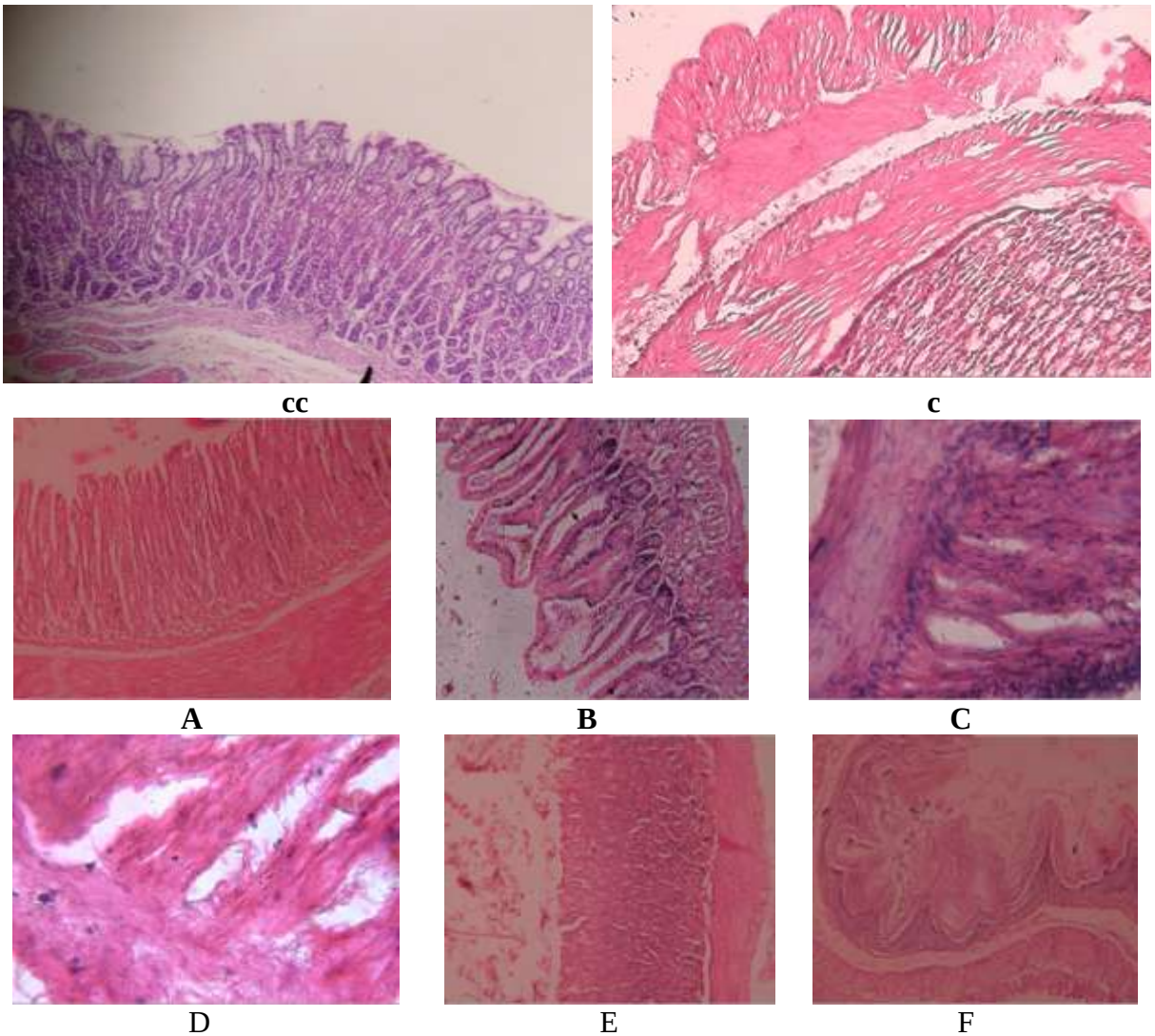
of groups A and B (treated with IDS @ 150mg/mouse and inoculated with a low dose of Gene Vac B vaccine @ 0.07 and 0.1 ml respectively). Experimental mice of groups C (0.2 ml of vaccine), D (0.4 ml of vaccine) and E (0.8 ml of vaccine), showed excessive secretion of mucus ; the layers of stomach and gastric folds were covered with mucus coating when compared to the control mice. The stomach exhibited slight damage in glandular epithelium of mucosa of gastric folds in animals of group F (1.0ml of vaccine).

Day 15: The stomach in mice of groups A, B, and C did not showed marked changes in its architecture , single doses of 0.4 (group D) , 0.8(group E) and 1.0 (group F) ml of vaccine showed slight destruction in gastric folds (glandular epithelium of the mucosa) ; whereas the other layers remained intact.

DISCUSSION

The ability of IDS when given with varied doses of Gene Vac B vaccine as an adaptogenic drug in adjuvant therapy might have evoked specific and non – specific immune responses in Swiss albino mice. Simultaneously heavy doses of the vaccines (group E and F) evoked stress in the experimental mice made the gastro-intestinal tract feeble and highly ulcerative which is accompanied by the signs of loss of appetite,

Figure 1: Showing the T.S of stomach on day 11 from control (group c) , IDS treated (cc) and experimental groups (A , B, C, D, E and F). All the panels are at 40X magnification



anorexia and complete asthenia. This condition in the stomach and large intestine may be the result of increased stress by producing excessive ROS species leading to increased SOD activity in liver and heightened LDH response in abdominal muscle. These findings correlate with that of Vardhani et al., (2011) and Nathanael and Vardhani (2014). Excessive secretion in the mucus , mucus coating on the stomach and gastric folds , slight to heavy necrosis in the test mice which received heavy doses of vaccine , and accumulation of cell debris in the lumen might be the result of the aberrational changes brought about by IDS and Gene Vac B vaccine in triggering the synthesis of proteins and DNA. These findings correlate with that of Anderson (1992) , Cuesta et al., (2003) and Petronov et al., (2007) who suggested the use of adjuvants boost up the mechanisms of molecular synthesis. These findings clearly confirm the work of Sakunthala et al ., (2014) and Nathanael and Vardhani (2014) where there is a heavy raise in proteins and DNA were manifested in stomach , large intestine and liver in mice treated with IDS and varied doses of Gene Vac B vaccine.

These changes clearly suggest that IDS when given orally is quickly absorbed and assimilated in the gastro-intestinal tract and stimulated synthesis of proteins and DNA there by there is infiltration of cells occurred and the accumulation of cell debris took place in the lumen of the stomach and large intestine. The varied doses of Gene Vac B vaccine might have increased the efficacy of Immunex DS (IDS) in the form of a better adjuvant holding responsible for extended immune response and upheavals in the molecular synthesis.

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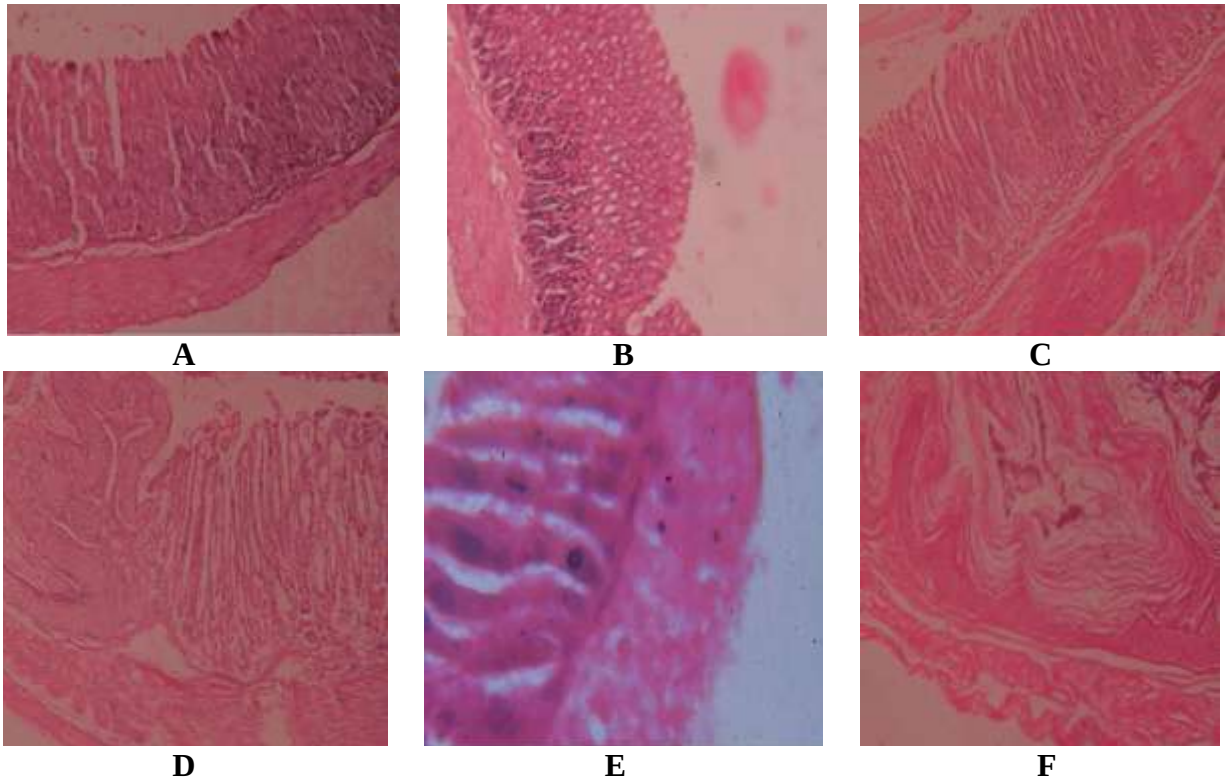
Figure 2: Showing the T.S of stomach on day 15 from control (group c) , IDS treated (cc) and experimental groups (A , B, C, D, E and F). All the panels are at 40X magnification



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