ORIGINAL ARTICLE

RESIDUAL LEVEL OF DELTAMETHRIN INDUCED GASTRITIS AND PREVENTIVE ROLE OF CURCUMIN ON STOMACH MUCOSA

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Background Benefits of Curcumin for health have been explained by different experimental models and clinical trials. It is a very potent antioxidant. Curcumin was found to play a preventive and curative role in both acute and chronic gastritis. Deltamethrin is a useful pesticide when applied with caution to crops. However, it also has noxious effects on gastric mucosa once ingested with sprayed crops. Its maximum permissible limit, MRL (Maximum Residual Level) as pesticide food residues is 5 mg/kg body weight as defined by WHO. However, there is still a potential to cause harm at these levels and maybe a serious potential health hazard. The present study aimed to: (a) determine the prevalence and severity of gastritis induced by deltamethrin when administered at MRL doses and (b) To observe the preventive effect on gastric mucosa against the action of Deltamethrin present as a residual pesticide in different vegetables and fruits. **Methods** In this two-phase subacute toxicity study of seven weeks, forty Sprague Dawley rats were divided into eight subgroups. Control groups were kept on a normal diet and sesame oil. Out of the two treatment groups, one group was given deltamethrin (5 mg/kg body weight) orally along with curcumin 100 mg/kg body weight. The second group was first given deltamethrin (5mg/kg body weight) and curcumin (200mg/kg). All were culled at its end. The stomach samples were collected and processed to obtain histology slides for analysis via microscopy and micrometry. Grading was done to look for changes according to the "Visual Analogue Scale and Operative Link on Gastritis Assessment (OLGA)". **Results** The experimental deltamethrin group when compared to control groups, revealed mild changes in stomach histomorphology while curcumin-treated both groups; Group D (100 mg/kg) and Group E (200 mg/kg) showed no changes. **Conclusion** Administration of Deltamethrin even in maximum residual dose (permissible) is proven to be toxic. Curcumin is hence proven to protect the gastric mucosa against the toxic effects of deltamethrin ingested in residual form.

Keywords: Deltamethrin; Gastritis, Stomach mucosa

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INTRODUCTION

The principal use of Deltamethrin (85% of the total production) is for crop protection (WHO: Environmental Health Criteria 97: Deltamethrin).[1] Deltamethrin is also used to protect stored food items such as cereals, grains, and coffee beans.[2] Other uses include insect control for public health concerns, pest control in forestry, pest control in animal facilities, parasite control on animals, and as a wood preservative.[3]

Humans if exposed to high doses either through oral route or dermal route, multiple systems can be affected. [4] In GI tract it causes nausea, vomiting, and diarrhoea. Central nervous system symptoms include ataxia, tremors, convulsions, paralysis, and irritability.[5] Miscellaneous symptoms include dermatitis, oedema, dyspnoea, rhinorrhoea, tinnitus, and even death due to respiratory failure. Allergic reactions range from dermatitis to even anaphylaxis.[6]

Deltamethrin on one side is very effective against various pests, but on the other hand is equally toxic for the human body. It has been determined that one of its main sources of exposure to the general population is the residues found in food. There are certain permissible levels of pesticide residue in these eatable items which are already determined by the World Health Organization (WHO). Some examples are mentioned in table 2. Tea is selected as a reference for this study because it has a maximum MRL among the different food items on which deltamethrin residues have already been determined (5mg/kg).[7]

Curcumin (*Curcuma longa*) is a polyphenolic compound and is a member of the ginger family (*Zingiberaceae*).[8] It is extracted from

the rhizomes of *Curcuma longa Linn* plant. It is one of the common curcuminoids present in turmeric.
The benefits of Curcumin for health have been explained by different experimental models and clinical trials. It is a very potent antioxidant.[9] Curcumin can be compared with Vitamin C and Vitamin E because it was proved that curcumin is ten times more potent than Vitamin E.[10] Curcumin also plays a role in reducing symptoms of Rheumatoid arthritis and Alzheimer's disease. [11] It helps in reducing the risk of Myocardial Infarction by preventing the platelets aggregation, and reducing the blood cholesterol level.[12] Curcumin was found to play preventive and curative roles in both acute and chronic gastritis[13], inflammatory conditions related to bowel like Crohn's disease and ulcerative colitis[14]. The previous clinical trials have already explored the Food item MRL Leafy vegetables 2 mg/Kg Whole Wheat 2mg/Kg Tea 5 mg/Kg Pulses 1mg/Kg. Chapter-1 Introduction 6 Therapeutic potential of curcumin in the gastrointestinal tract because of its high bioavailability as compared to other organs and those include gastritis caused by *H. pylori,* [15], [16], some functional digestive disorders, colorectal cancer and liver disease. [17] Thus knowing about all these benefits the current study focuses on one of the best-explored actions of curcumin, i.e., its curative and preventive effect on gastric mucosa against the action of Deltamethrin present as a residual pesticide in different vegetables and fruits.

This histo-morphological study is thus conducted to see the morphological changes (if any) in the gastric mucosa caused by the residual amount of Deltamethrin present in the food items. And to study the preventive role of Curcumin against deltamethrin induced gastric damage.

MATERIAL AND METHODS

The proposal for this study was approved in the 36th meeting of the Advanced Study and research board (AS&RB) under No. DIR/KMU-ASRB000457/HR/IBMS. The study was conducted under the guidelines of the Ethical committee of Khyber Medical University Peshawar. The ethical board approved it under No. "DIR/KMU-EB/HR/000284". I followed ARRIVE guidelines and the 3 R's of FRAME protocol. Ten (10) Healthy albino (Wistar) rats, Rattus norvigattus, with an average weight of 280gms and aged between 8-12 weeks were purchased from the National Institute of Health (NIH) Islamabad. It was an Experimental lab-based Study. The sampling technique was simple Random sampling technique. In this study, two different strengths of curcumin 100 mg/kg for group "D", and 200 mg/kg for group "E" was used along with Deltamethrin 5 mg/kg body weight per day. Final observations were analysed according to standard scoring systems, divided into two levels:
Basic Level**:** Visual analogue scale was applied. According to this scale, a Maximum of 5 lymphocytes, plasma cells and macrophages per high-power (x40 objective) is considered "Normal"[18,19] Neutrophils are usually do not present in non-inflammatory conditions[20].

Advance Level**:** In the advanced level the extent of glandular atrophy is observed and classified as mild moderate and severe. This classification is according to the international system for gastritis scoring "operative link on gastritis assessment (OLGA)".[21] OLGA scoring is done to see the atrophy of the glandular apparatus. First, the percentage of atrophy is observed at the compartment level and then all the compartments to get the total OLGA score.[22]

Table-2: Details of Groups in phase 1 and phase 2 and their dosages

Groups	No. of Rats (Total)	Period (28 days)
Group-A Control	6	Normal Diet + Vehicle (Sesame oil) by oral gavage
Group-C	4	Deltamethrin (5 mg/kg/day) by oral gavage
Group-D	4	-Deltamethrin (5 mg/kg/day) + Curcumin (100 mg/kg/day) by oral gavage
Group-E	4	-Deltamethrin (5 mg/kg/day) + Curcumin (200 mg/kg/day) by oral gavage

RESULTS

To observe the preventive effects of curcumin Group D was administered 100mg/kg/day curcumin along with 5mg/kg/day Deltamethrin simultaneously. Group E was given 200mg/kg/day. Results were analyzed by visual analogue scale and Olga scoring system as explained above. Groups D and E showed "NO" inflammatory changes and there were occasional lymphocytes and monocytes (less than five cells per field). Neutrophils were not present and hence there was no sign of acute or sub-acute inflammatory changes.

OLGA (atrophy scoring) No atrophy was observed in Group D and E. Morphology of glands was preserved in both oxyntic and antral areas. This clearly explains that curcumin has a very strong preventive effect on gastric mucosa. (ANOVA < 0.001. Sections of the corpus and antrum are given in Figure 2

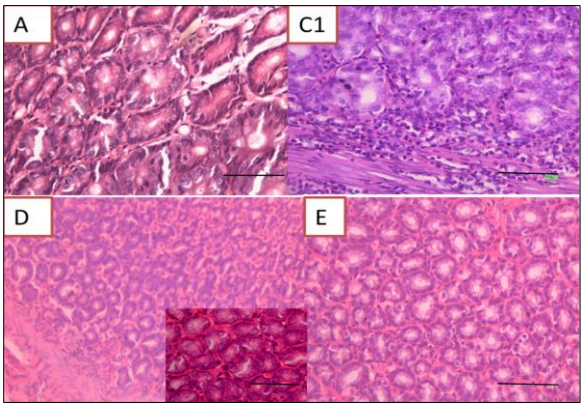

Figure-1: C/S of Gastric glands. Showing no inflammatory cells in Group A. mild to moderate inflammatory cells with prominent neutrophils in Group C1. No Neutrophils in Group D and E. H&E stain. 40 X.

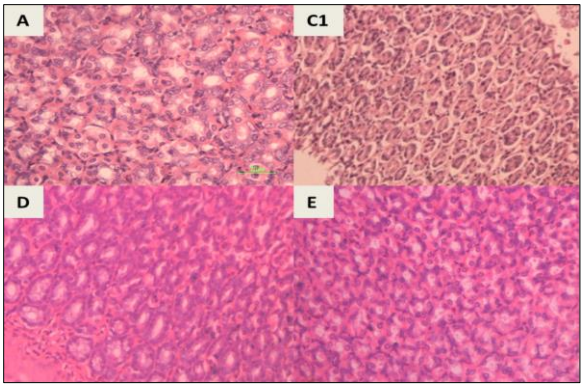

Figure-2: Cross section of corpus showing A; Normal histology. Deltamethrin(C1); mild atrophy. D and E showed normal histomorphology of fundic glands. (High magnification; scale: 2µm)

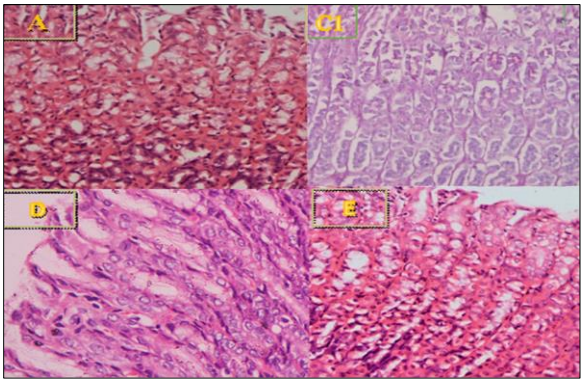

Figure 3-: Longitudinal section of antrum: Showing histomorphology of antral glands. Group C1 shows mild atrophy of antral glands. Group D and E showed normal morphology of glands when compared with control group A. (H&E; scale=10µm)

DISCUSSION

The primary aim of this study was to examine the effects of pesticide (Deltamethrin) in its residual form on our stomach mucosa which are entering in our body along with our routinely ingested food and then to observe the curative and preventive effects of curcumin on gastric mucosa. For this purpose, the rodents were grouped according to the plan (table 2). Results of our study revealed that Deltamethrin when given orally even in residual quantity caused significant damage to the gastric tissue in phase one. The amount of damage was measured by the visual analogue scale for inflammatory infiltrates and atrophy of glands was measured by OLGA score Cumulative result of the Deltamethrin treated group was labelled as "mild atrophy" according to the Visual Analogue scale and Operative Link on Gastritis assessment. Our study also shed light on the gastro curative and gastro protective effects of Curcumin. Curcumin also had preventive effects on the stomach when given along with Deltamethrin in phase 1 to Group D and E. Both groups D and E showed no inflammatory cells according to the Visual Analogue Scale. Thus the preventive effect is slightly better in higher doses of curcumin treated group (E). In 2013, the protective effects of curcumin was studied against the vulnerable indomethacin[23] and discovered that Curcumin increases the mucin component of gastric tissue, moreover, their results explained the decrease in total acid output and revealed that Curcumin protects the gastric mucosa by increasing the gastric mucosal barrier and decreasing the quantity of acid produced. Another study published in 2016 revealed the protective effects of curcumin against the adverse effects of ethanol.[24] But they did not grad inflammatory changes in the stomach. Results of their ethanol + curcumin treated group revealed significant gastro protective action of Curcumin as there was no inflammatory changes present in gastric mucosa. Thus their cumulative data showed that curcumin is an important protective agent in the pathogenesis of gastritis caused by ethanol. Our study can be compared with Hasan Turkez's study which was published in 2012.[25] In which the protective effects of Olive leaf extract was explained against the oxidative stress caused by permethrin. It was an experimental lab-based study; in one group he administered permethrin in a dose of 60mg/kg. In another group, he administered olive leaf extract in a dose of 500mg/kg along with permethrin. Permethrin revealed oxidative stress while olive leaf extract significantly reduced those harmful effects of permethrin in the second group. In our study, we used residual pesticide amount as compared to the toxic doses and Curcumin instead of Olive leaf extract as a preventive agent. Curcumin has also proved itself by managing and avoiding the inflammatory process in periodontitis Curcumin has efficient anti-bacterial activity against *P. gingivalis* infection and biofilm formation. Besides anti-oxidant antibacterial and

anti-inflammatory action, it has some immunosuppressant properties as well via the suppression of Th17 pro-inflammatory responses and enhancing the regulatory T cells, thus inhibiting autoimmunity.[26] There were some unavoidable limitations. First, in our study an addition of a "curcumin only" group to observe the effects of "curcumin" on a normal stomach may be suggested but because of various studies indicating the beneficial effects of curcumin it did not seem feasible. The second limitation was that the sample size was small which created a large standard deviation in our statistical analysis. This was due to less number of available albino rats at that time. For a larger sample size we had to wait for a few months and still, there was no assurance of availability and mainly a time limitation to the study. In spite of these we have identified significant changes and results but increasing sample size would increase the robustness of the study.

AUTHORS' CONTRIBUTION

AH: Conduction of research, literature and data collection. WA: Study design, data interpretation. HI: Proofreading. MJ: Concept. HA: data analysis.

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