

ANTIULCER EFFECTS OF AGOMELATINE AND ITS POTENTIATION WITH PYRIDOXINE

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ABSTRACT

Agomelatine is a manufactured simple of melatonin and a strong agonist of melatonin receptors. Agomelatine has Hepatoprotective just as cancer prevention agent action. The point of study was to assess the antiulcer action of Agomelatine and its potentiation through the pyridoxine on ethanol initiated gastric ulcer in rodents.

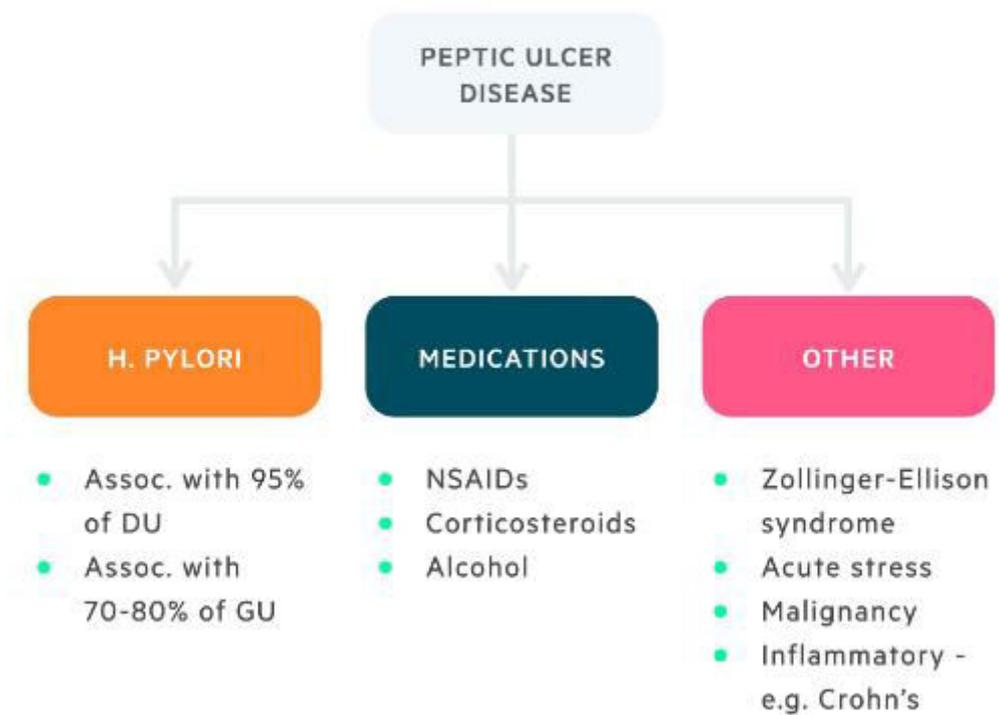
Methods: Thirty number of rodents were separated in to five gatherings contro, standard, Agomelatine low portion, Agomelatine high portion and Agomelatine with Pyridoxine gatherings. Ethanol was utilized to prompted gastric ulcer in rodents. ulcer record and furthermore the other biochemical boundaries like free Acidity, complete Acidity, gastric pH, volume of gastric juice was resolved. Measurably examination was finished by ANOVA P esteem under 0.05 was viewed as statistically significant.

Results: In the current investigation, an endeavor has been made to research the gastric antisecretory, antiulcer and cytoprotective properties of agomelatine. The outcomes are genuinely huge by ANOVA test. Ranitidine showed a measurably critical reduction in the volume of gastric juice by free corrosiveness and complete sharpness. when contrasted with control. Agomelatine shows a showed comparable reaction to the volume of gastric juice. A huge distinction in pH was seen between the agomelatine-treated, agomelatine with pyridoxine treated gathering and the control groups. **Conclusions:** Pretreated rodents with Agomelatine (40 milligram/kg) showed defensive impact against ethanol actuategastric ulcer. Agomelatine (40 milligram/kg) showed the ameliorative impact with Pyridoxine (0.3 milligram/kg), on gastric ulcer.

Keyword-Agomelatine, Pyridoxine, Antiulcer, H.pylori

INTRODUCTION

Ulcer is characterized as disturbance of the mucosal respectability of the stomach and additionally duodenum prompting a neighborhood imperfection or exhuming because of dynamic irritation. Ulcers happen inside the stomach as well as duodenum and are frequently persistent in nature. Peptic ulcers are open injuries in the upper piece of the stomach related part that can cause stomach torture or stomach upset, and that can provoke inside biting the dust. Stomach ulcers improvement happens with corrosive and breakdown of mucosal safeguard uncontrolled corrosive emission and ulcerodentation of the stomach mucosa because of a few reasons have presented major issues to the human wellbeing everywhere on the world (Khalil et al., 2010). Epidemiological information for this infection, and its complications have demonstrated striking topographical varieties in rodente and pervasiveness.^{1,2}



FigNo: 1. Causes of Peptic Ulcer Deceases

There are two kinds of peptic ulcers:

- Stomach ulcers, which structure on the coating of the stomach.
- Duodenal ulcers, which structure on the coating of the upper piece of the small digestive tract (called the "duodenum").

Classification

- [1] In Duodenum duodenal ulcer
- [2] In Stomach stomach ulcer
- [3] In Esophagus Oesophageal ulcer.

Agomelatine is a creative upper as of late authorized by the many Medicines Agency for the therapeutic management of significant burdensome scenes in grown-ups. Its consolidated activities at MT1, MT2, and 5HT-2C receptors can improve the upset circadian musicality and unusual rest design subsequently produce the energizer impact. These remarkable impacts propose that it very well may be viable for the treatment of occasional emotional problem like uneasiness and bipolar despondency. Agomelatine is a productive restorodentive alternative in significant burdensome problem determined in patients to have diabetes mellitus, as it diminishes the seriousness of full of feeling indications and expands the worldwide working, without negative impacts over the body weight or glucose levels. Agomelatine has a quicker beginning of activity in the rest disturbancies than SSRIs and is by all accounts preferable endured over **fluoxetine (Vasile. et al., 2008)**.^{3,4}

Karakus et al., 2013, assess the hepatoprotective movement of agomelatine on paracetamol-instigated hepatotoxicity and to comprehend the connection between the hepatoprotective instrument of agomelatine and cancer prevention agent framework and proinflammatory cytokines, and they reasoned that the organization of Agomelatine (40mg/kg) shields liver cells from paracetamol-prompted hepatotoxicity through cell reinforcement action and diminished proinflammatory cytokines, for example, TNF- α and IL-6. **Morera-Fumero et al., 2009** concluded the instancebehavior of a schizophrenic population with extreme sleep deprivation that had an incomplete reaction to high portions of benzodiazepines and quieting antipsychotics. Promptive management with agomelatine permitted suspending benzodiazepine treatment and reestablishing nature of rest.^{5,6}

MATERIALS AND METHODS

Experimental Rodents

Wistar albino rodents of either sex weighing between 150-200g were used for this study. They were procured in the institute of pharmaceutical science and research,(IPSR) unnao recognized by the Institutional Animal Ethics Committee (IAEC). Polypropylene limits were used to house (3 for each pen) the animal at a temperature of 28 \pm 50C and 12 h light /dull cycle. Hindustan Lever chow pellets were used to feed the animal and water not basic. The animals were kept fasting medium –term going before the examination and this study was approved by IAEC for animal studies include all framework used in the research.

Drugs and Chemicals

Agomelatine was acquired from Precise Chemipharmapvt. Ltd (Navi Mumbai), Ranitidine hydrochloride and pyridoxine were mercifully given by Sigma Chemical Co, were totally suspended in 0.5% Xanthan Gum suspension.

Preparation of Drugs

For the trial reason, Agomelatine (Precise chemipharmapvt.ltd, Navi Mumbai) and Ranitidine hydrochloride (Sigma Chemical Co) were suspended in 0.5% Xanthan Gum suspension, utilizing a Magnetic Stirrer to get a homogenous suspension. Pyridoxine was broken down in refined water, utilizing a magnetic Stirrer to get a homogenous arrangement. New medications suspensions were set up on every day of the trials. Medications were regulated orally agreeing the creature body gauge

Preparation of Xanthan Gum (Vehicle)

0.5% Xanthan Gum was set up by adding 0.5 g of Xanthan Gum to 100 mL of refined water.

STUDY DESIGN

Ethanol Induce Ulcer.

Procedure

Sound Wistar rodents of weighting between 210-260 gm were taken for the investigations. The creature were separated in to five gatherings (each contain 6 creatures) as follow-

Gathering –V : Agomelatine and Pyridoxine (0.milligram/kg) x 6

Gathering– IV : Agomelatine (40 milligram/kg) x 6

Gathering – III: Agomelatine (30 milligram/kg) x 6

Gathering – II (Standard): Ranitidine (200 milligram/kg) x 6

Gathering – I (Control): Vehicle x 6

The creatures were arbitrarily separated in to five gatherings and abstained for 24 h before the examination. On day 5, the creatures of II, III, IV and V were orally controlled with ranitidine (200mg/kg), Agomelatine (30 mg/kg), Agomelatine (40 mg/kg), Agomelatine and Pyridoxine (0.3 mg/kg) individually, 1 hr. before organization of 1 ml total ethanol. One hour after organization of ethanol, the creatures were euthanized with CO₂, the stomachs were disconnected and cut along the more noteworthy arch, ulcer score was finished. Stomach juice was gathered and stomach

emissions contemplated were played out .The number and seriousness of ulcers is enlisted with a sound system magnifying instrument utilizing the accompanying scores:

Scoring of ulcer.^{7,8}

3 = Ulcers >5.

2 = Ulcers ≥ 3 but ≤ 5 .

1.5 = Haemorrhagic streaks.

1 = Spot ulcer.

0.5 = Red colourodentation.

0 = Normal coloured stomach.

Calculation of ulcer Index (Vogel et al., 2002) $U_I = U_N + U_S + U_P \times 10^{-1}$

U_P = percentage of creatures with ulcers.

U_I is representation for Ulcer Index.

U_N is representation for Average of number of ulcers per creature.

U_S is representation for average of severity score.

Stress Ulcer through Immobilization Stress

Healthy Wistarrodents of weighting between 210-260gm were taken for the studies.

The creature were grouped in to five groups (each contain 6 creature) as follow-

Gathering –V : Agomelatine and Pyridoxine (0.milligram/kg) x 6

Gathering– IV : Agomelatine (40 milligram/kg) x 6

Gathering – III: Agomelatine (30 milligram/kg) x 6

Gathering – II (Standard): Ranitidine (200 milligram/kg) x 6

Gathering – I (Control): Vehicle x 6

The creatures were haphazardly partitioned in to five gatherings and abstained for 24 h before the analysis. On day 5, the creature of II, III, IV and V were orally managed with ranitidine (200mg/kg), Agomelatine (30 mg/kg), Agomelatine (40 mg/kg), Agomelatine and Pyridoxine (0.3 mg/kg) separodentely, after 1 hr. creatures are enclosed by wire look. They are evenly suspended in obscurity at 20 °C for 1 hr. lastly forfeited in CO2 sedation.

The stomachs were secluded and cut along the more noteworthy ebb and flow, ulcer score was finished. Stomach juice was gathered and stomach discharges considered were played out .The number and seriousness of ulcers is enrolled with a sound system magnifying instrument utilizing the accompanying scores:⁹

Scoring Of Ulcer

3 = Ulcers >5.

2 = Ulcers ≥ 3 but ≤ 5 .

1.5 = Haemorrhagic streaks.

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Calculation of ulcer Index

$$U_I = U_N + U_S + U_P \times 10^{-1}$$

U_P = percentage of creatures with ulcers.

U_I is representation for Ulcer Index.

U_N is representation for Average of number of ulcers per creature.

U_S is representation for average of severity score.

Assessment of Stomach Mucosal Lesions

The creatures were euthanized with CO₂, One hour after organization of ethanol. Each stomach was taken out and opened along the more noteworthy ebb and flow, and the stomach juice was gathered. The stomachs were washed with super cold saline and inspected for perceptibly. The stomach mucosal injuries were communicated regarding ulcer file (U.I.), which relies upon the count of a sore record by utilizing a scoring framework dependent on the seriousness of every sore. The seriousness factor was characterized by the length of the sores. Severity factor 0 = no lesions; 1 = lesions < 1 mm length; 2= lesions 2-4 mm length and 3 = lesions > 4 mm length.

Analysis of Stomach Juice

Stomach juice gathered from every creature and centrifuged at 2500-3500 rpm for 10 min to eliminate all strong garbage and the content of the supernatant was estimated. The supernatant material was then inspected for the various parameter and also for pH, Free and absolute corrosive.¹

Determination of Free and Total Acidity

One milliliter of stomach juice was separated out in to a 100 ml volumetric flask, prescribed quantity of Topfer's reagent were mixed and this was analysed with 0.01 N Sodium hydroxide until all hints of Red shading vanished and the shade of the arrangement become Yellowish-Orange in titration. The quantity of soluble base required base to complete the reaction was noted. This volume relates to free acidity. At last of phenolphthalein arrangement was mixed and tabulate end point. The complete volume of soluble base added was noted. The volume relates to add up to corrosiveness.

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$$\text{Acidity} = \frac{\text{Volume of NaOH} \times \text{Normality of NaOH} \times 100}{0.1} \text{ Meq/lit/100gm}$$

Histopathological Studies

The stomach and Brain from all gatherings were eliminated quickly, opened along the more noteworthy arch, and altogether flushed with super cold saline. Subsequent to recording the ulcers delivered in the stomach, a specific longitudinal section of the particular stomach location was taken from the front piece of the stomach and in continuation in experiment Brain with particular parts was fixed in a formalin 10% arrangement. After twenty four hour of obsession counter by inserting in a paraffin block, it was cut into areas of 5 micron on to a clear vision glass plate and stained with hematoxylin-eosin for histological evaluation of the GIT section.

Statistical Analysis

Measurable investigation in all the above examinations was performed utilizing Graph Pad Prism programming. All outcome were communicated as mean \pm S.E.M. Information were broke down utilizing single direction investigation of fluctuation (ANOVA), and followed by Dennet's different examination tests. Worth $P < 0.05$ and underneath were viewed as huge.

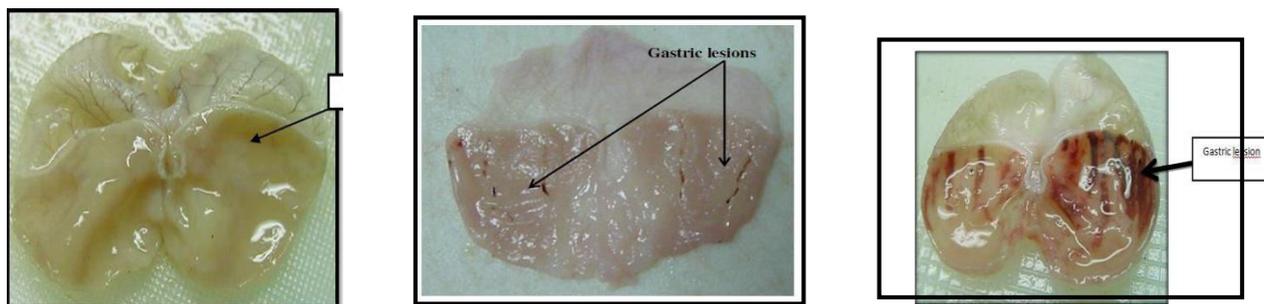
RESULTS AND DISCUSSION

Intrastomach organization of one ml ethanol reliably caused hemorrhagic sores in the mucosa of the glandular stomach. The benchmark group indicated ulcerodentation, redness, and hemorrhagic streaks, after ethanol organization. There was likewise an increment in stomach pH (Table .1), and lessening in stomach volume (Table .2), Ulcer Index (Table.4) free corrosiveness (Table .5), and complete acidity (Table.6). Agomelatine (40mg/kg portion, with Pyridoxine at 0.3mg/kg portion), and Ranitidine produce huge ($P < 0.05$) decrease in ulcer score (Table 8) when contrasted with the control.

Gross Evaluation of Stomach Lesions

The counter ulcer movement of Agomelatine in ethanol-instigated stomach sore and Stress ulcer through immobilization stress models are accounted for in Tabular structure. Results indicated that rodents pre-treated with Agomelatine prior to being given outright liquor had fundamentally decreased regions of stomach ulcer arrangement contrasted with rodents pre-treated with just 0.5% Xanthan Gum suspension (ulcer control gathering).

Besides, the Agomelatine altogether stifled the development of the ulcers. It was likewise seen that assurance of stomach mucosa was more noticeable in rodents pre-treated with Agomelatine (Figure No. 2) and Pyridoxine. Close to, ethanol-instigated mucosal harm was altogether and portion conditionally diminished in the size and seriousness by pretreatment of the creatures with Agomelatine. The critical restraint of stomach ulcer in pretreatment with Agomelatine was contrasted and Ranitidine which is a standard medication utilized for restoring stomach ulcer.¹¹



A. Control Group B. Agomelatine Group C. Standard Group

FigNo: 2 Macroscopic evaluation of Ethanol induce ulcer

5.2 Antiulcer Activity of Alone Agomelatine and Together With Pyridoxine

5.2.1 Ethanol Induce Stomach Ulcer

Table:- 6.1 Impact of Agomelatine, Pyridoxine, and Ranitidine pretreatment on Stomach pH in Ethanol actuate stomach ulcer in rodents.

Control group		LD Group(30 mg/kg)		HD Group(40 mg/kg)		Pyridoxine Group (0.3mg/kg)		Standard Group(200mg/kg)	
Male	1	Male	2	Male	2	Male	3	Male	3
Male	1	Male	3	Male	3	Male	3	Male	4

Male	2		Male	2		Male	3		Male	3		Male	3	
Mean±SEM			Mean±SEM			Mean±SEM			Mean±SEM			Mean±SEM		
1.3±0.0			2.33±0.3			2.66±0.0			3.0±0.033			3.33±0.33		
Female	1		Female	2		Female	3		Female	3		Female	4	
Female	1		Female	2		Female	2		Female	3		Female	4	
Female	1		Female	2		Female	3		Female	4		Female	4	
Mean±SEM			Mean±SEM			Mean±SEM			Mean±SEM			Mean±SEM		
1.3±0.0			2.0±0.33			2.66±0.33			3.33±0.33			4.0±0.33		

Values are shown as mean ± SEM, n=6; The mean distinction is critical at P estimation of < 0.05.

Results indicated that rodents pre-treated with Agomelatine prior to being given total liquor had altogether increment the stomach pH, contrasted with rodents pre-treated with just 0.5% Xanthan Gum suspension (ulcer control gathering).

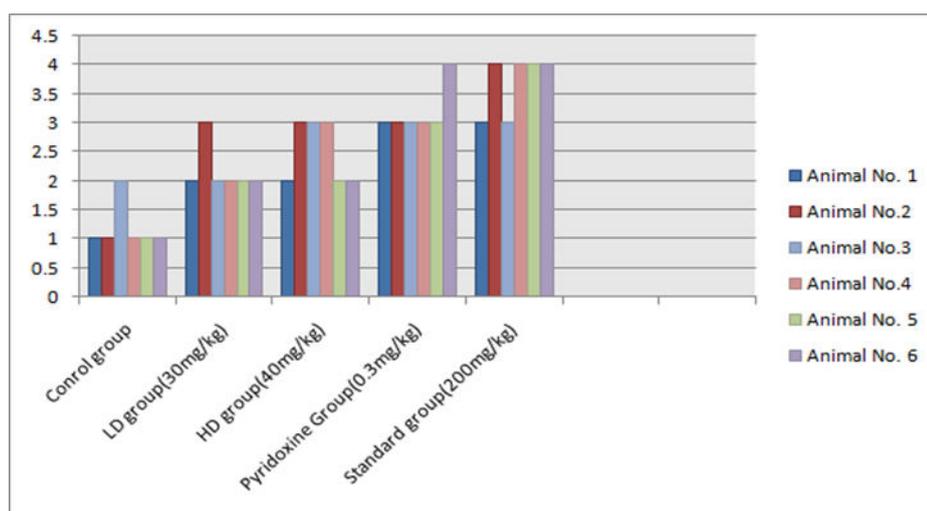


Fig No. 3 Effect of Agomelatine and its mix on Stomach pH prompt by Ethanol

Table:-.2 Impact of Agomelatine, Pyridoxine, and Ranitidine pretreatment on Stomach Volume in Ethanol actuate stomach ulcer in rodents

ControlGroup		LDGroup (30mg/Kg)		HDGroup (40mg/Kg)		PyridoxineGroup (0.3mg/Kg)		StandardGroup (200mg/Kg)	
Male	2.5	Male	1.8	Male	1.6	Male	1.3	Male	0.8
Male	2.8	Male	2.6	Male	1.8	Male	1.4	Male	0.6
Male	3.1	Male	1.8	Male	1.7	Male	1.5	Male	0.5
Mean±SEM		Mean±SEM		Mean±SEM		Mean±SEM		Mean±SEM	
2.8±0.2		2.0±0.2		1.7±0.5		1.4±0.5		1.0±0.08	

Female	3.5	Female	1.9	Female	1.9	Female	1.8	Female	0.6
Fema Le	2.6	Female	2.2	Female	1.8	Female	1.5	Female	1.2
Female	2.1	Female	2.0	Female	1.8	Female	1.6	Female	0.8
Mean±SEM	2.7±0.4	Mea±SEM	2.0±0.8	Mean±SEM	1.9 ±0.05	Mean±SEM	1.6±0.8	Mean±SEM	0.86±0.1

Values are shown as mean ± SEM, n=6; The mean distinction is critical at P estimation of < 0.05.

Results indicated that rodents pre-treated with Agomelatine prior to being given total liquor had fundamentally decreased the stomach Volume, contrasted with rodents pre-treated with just 0.5% Xanthan Gum suspension (ulcer control gathering).

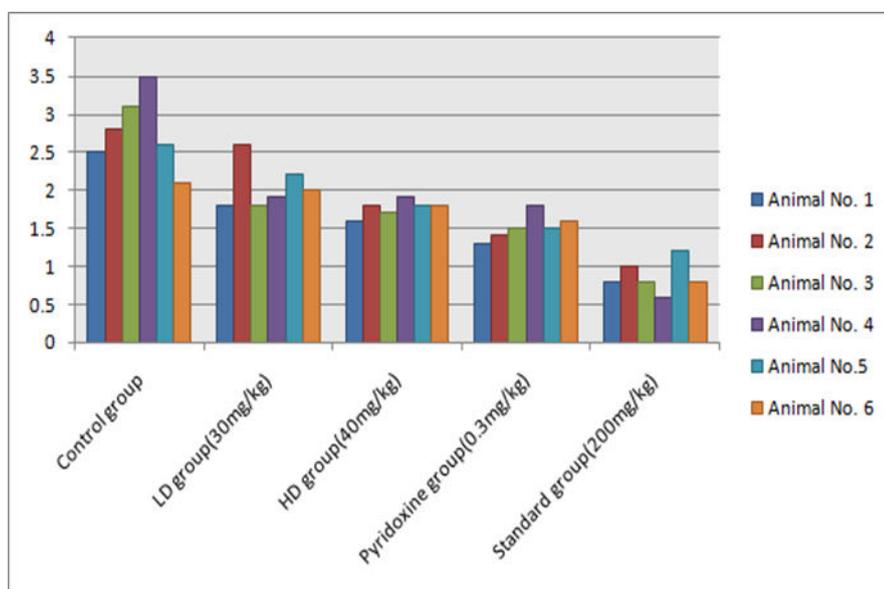


Fig No:- 4Effect of Agomelatine and its combination on Stomach Volume induce by Ethanol.

Table: - 3 Impact of Agomelatine, Pyridoxine, and Ranitidine pretreatment on StomachScore in Ethanol actuate stomach ulcer in rodents.

ControlGroup		LD Group(30 mg/Kg)		HD Group(40 mg/Kg)		Pyridoxine Group(0.3 mg/Kg)		Standard Group(200mg /Kg)	
Male	2	Male	1.5	Male	1	Male	0.5	Male	0.5
Male	2	Male	1.5	Male	1	Male	0.5	Male	0.5
Male	1.5	Male	1	Male	0.5	Male	1	Male	0.5
Mean±SEM 1.83±0.2		Mean±SEM 1.33±0.16		Mean±SEM 0.83±0.16		Mean±SEM 0.66±0.16		Mean±SEM 0.5±0.00	
Female	1.5	Female	1	Female	0.5	Female	1	Female	0.5
Female	1.5	Female	1	Female	0.5	Female	0.5	Female	1
Female	2.0	Female	1.5	Female	1.0	Female	1	Female	0.5
Mean±SEM 1.66±0.16		Mean±SEM 1.2±0.16		Mean±SEM 0.66±0.16		Mean±SEM 0.83±0.16		Mean±SEM 0.66±0.16	

Values are shown as mean ± SEM, n=6; The mean distinction is critical at P estimation of < 0.05.

Results demonstrated that rodents pre-treated with Agomelatine prior to being given total liquor had essentially diminished the Ulcer score, contrasted with rodents pre-treated with just 0.5% Xanthan Gum suspension (ulcer control gathering).

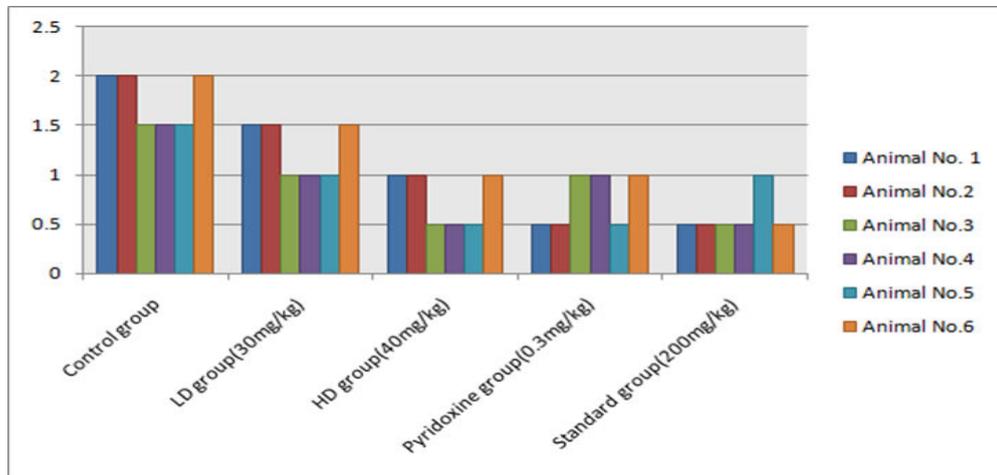


Fig No. 5-Effect of Agomelatine and its combination on Ulcer Score induce by Ethanol.

Table: - .4 Impact of Agomelatine, Pyridoxine, and Ranitidine pretreatment on Stomachulcer Index in Ethanol actuate stomach ulcer in rodents..

ControlGroup		LD Group(30 mg/Kg)		HD Group(40 mg/Kg)		Pyridoxine Group(0.3 mg/Kg)		Standard Group(200mg /Kg)	
Male	5.8	Male	3.2	Male	3.2	Male	2.8	Male	2.0

Male	5.7	Male	3.4	Male	3.4	Male	2.4	Male	2.2
Male	6.0	Male	4.8	Male	3.5	Male	2.2	Male	2.4
Mean±SEM 5.8±0.8		Mean±SEM 3.8±0.5		Mean±SEM 3.3±0.08		Mean±SEM 2.8±0.17		Mean±SEM 2.2±0.11	
Female	6.2	Female	3.8	Female	3.6	Female	2.8	Female	2.2
Female	5.4	Female	3.6	Female	3.2	Female	2.6	Female	2.2
Female	5.6	Female	4.2	Female	3.4	Female	2.0	Female	2.3
Mean±SEM 5.7±0.24		Mean±SEM 3.8±0.17		Mean±SEM 3.4±0.11		Mean±SEM 2.4±0.24		Mean±SEM 2.1±0.08	

Values are shown as mean ± SEM, n=6; The mean distinction is critical at P estimation of < 0.05.

Results indicated that rodents pre-treated with Agomelatine prior to being given total liquor had essentially decreased the Ulcer list, contrasted with rodents pre-treated with just 0.5% Xanthan Gum suspension (ulcer control gathering).

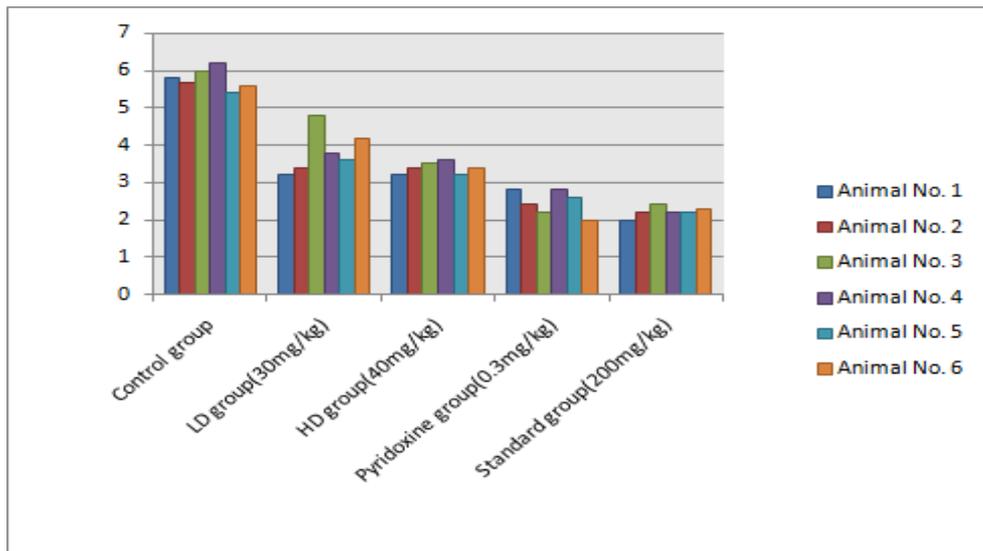


Fig No. 6 Effect of Agomelatine and its combination on Ulcer Index induce by Ethanol

ControlGroup		LD Group(30 mg/Kg)		HD Group(40 mg/Kg)		Pyridoxine Group(0.3 mg/Kg)		Standard Group(200mg /Kg)	
Male	22	Male	18.2	Male	12.3	Male	11.8	Male	9.6

Male	21	Male	16.2	Male	13.7	Male	12.0	Male	9.8
Male	24.2	Male	19.2	Male	12.0	Male	12.2	Male	10.1
Mean±SEM 22.4±0.90		Mean±SEM 17.86±0.88		Mean±SEM 12.66±0.52		Mean±SEM 12.0±0.11		Mean±SEM 9.8±0.14	
Female	22.4	Female	21.2	Female	12.8	Female	11.9	Female	10.2
Female	23.3	Female	20.0	Female	14.2	Female	11.3	Female	9.2
Female	20.2	Female	16.1	Female	12.6	Female	12.8	Female	9.8
Mean±SEM 21.96±0.9		Mean±SEM 19.1±0.5		Mean±SEM 13.2±0.5		Mean±SEM 12.0±0.43		Mean±SEM 9.7±0.29	

Table.:5 Impact of Agomelatine, Pyridoxine, and Ranitidine pretreatment on free acidity in stressactuatestomach ulcer in rodents.

Values are shown as mean ± SEM, n=6; The mean distinction is critical at P estimation of < 0.05.

Results indicated that rodents pre-treated with Agomelatine prior to being given supreme liquor had altogether decreased the Free sharpness, contrasted with rodents pre-treated with just 0.5% Xanthan Gum suspension (ulcer control gathering).

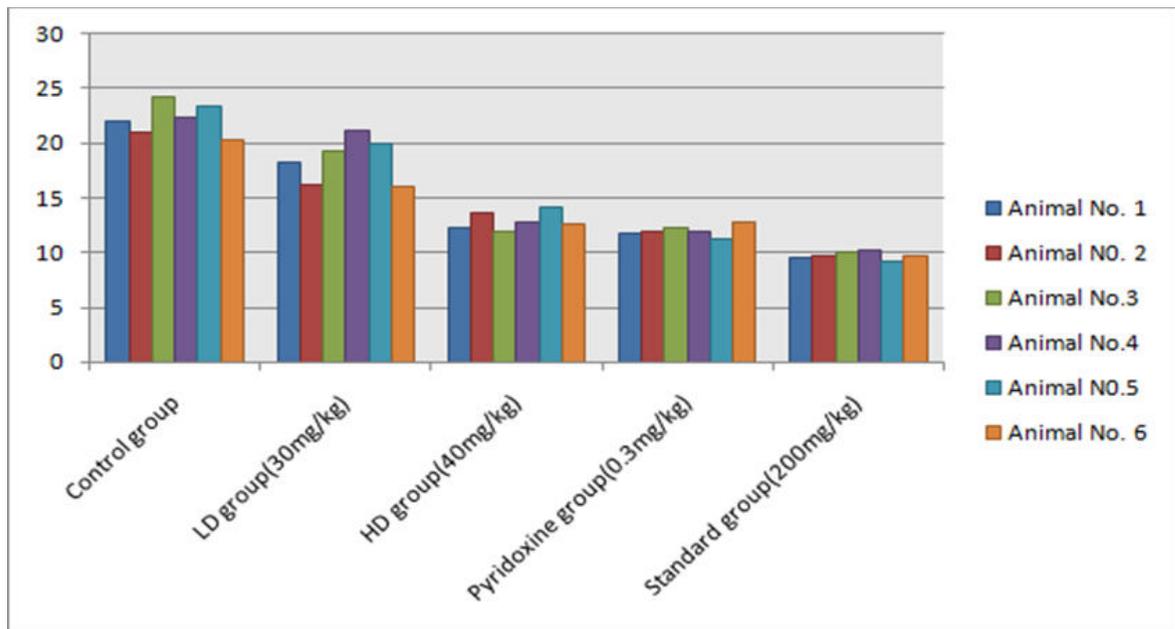


Fig No: 7 Effect of Agomelatine and its combination on Free Acidity induce by EthanolStress Ulcer through Immobilization Stress

Table: 6.Impact of Agomelatine, Pyridoxine, and Ranitidine pretreatment on Stomach pH in Stress actuatestomach ulcer.

Control Group		LD Group(30 mg/kg)		HD Group(40 mg/kg)		Pyridoxine Group(0.3 mg/kg)		Standard Group(200mg /kg)	
Male	1	Male	2	Male	2	Male	4	Male	3
Male	1	Male	3	Male	3	Male	3	Male	4
Male	2	Male	2	Male	3	Male	3	Male	4
Mean±SEM 1.3±0.0		Mean±SEM 2.33±0.3		Mean±SEM 2.66±0.0		Mean±SEM 3.0±0.033		Mean±SEM 3.33±0.33	
Female	1	Female	2	Female	3	Female	4	Female	4
Female	1	Female	2	Female	2	Female	3	Female	4
Female	1	Female	2	Female	3	Female	3	Female	4
Mean±SEM 1.3±0.0		Mean±SEM 2.0±0.33		Mean±SEM 2.66±0.33		Mean±SEM 3.33±0.33		Mean±SEM 4.33±0.33	

Values are shown as mean ± SEM, n=6; The mean distinction is critical at P estimation of < 0.05.

Results indicated that rodents pre-treated with Agomelatine before stress had altogether increment the stomach pH, contrasted with rodents pre-treated with just 0.5% Xanthan Gum suspension (ulcer control gathering).

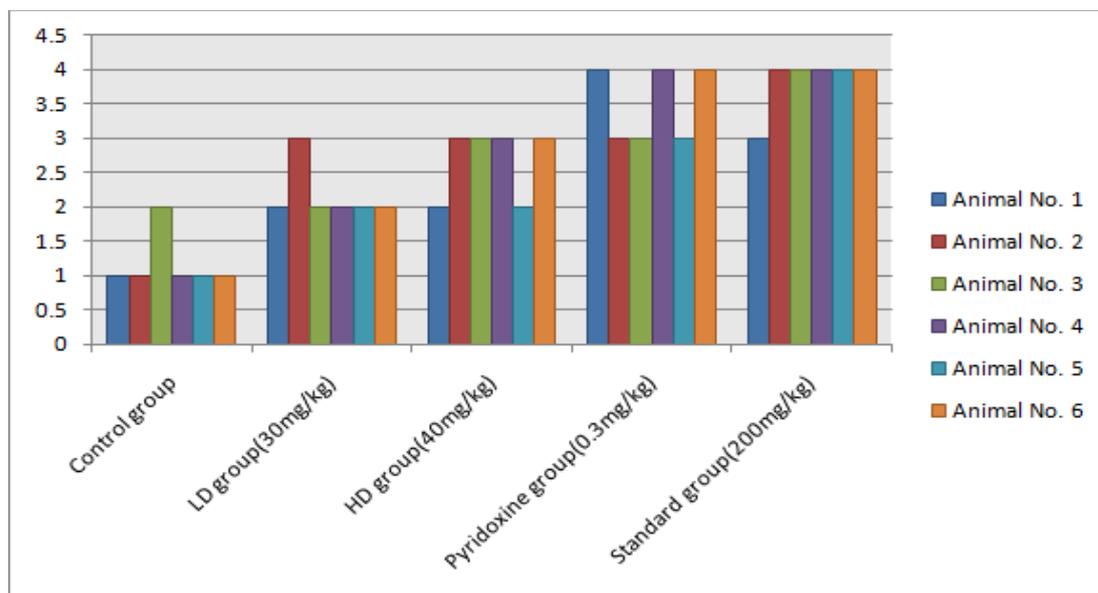


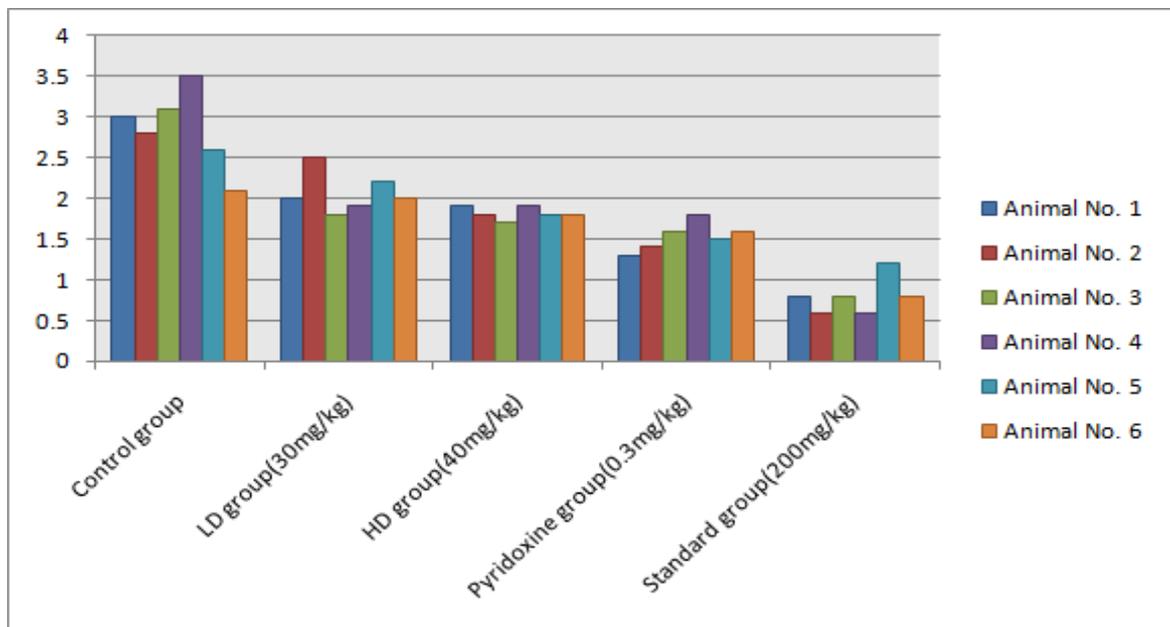
Fig No: 8-Effect of Agomelatine and its combination on Stomach pH induce by Stress.

Table: - 7Impact of Agomelatine, Pyridoxine, and Ranitidine pretreatment on Stomach Volume in Stress actuate stomach ulcer in rodents.

Control Group		LD Group(30 mg/Kg)		HD Group(40 mg/Kg)		Pyridoxine Group(0.3mg/Kg)		Standard Group(200mg/Kg)	
Male	3.0	Male	2.0	Male	1.9	Male	1.3	Male	0.8
Male	2.8	Male	2.5	Male	1.8	Male	1.4	Male	0.6
Male	3.1	Male	1.8	Male	1.7	Male	1.6	Male	0.8
Mean±SEM 2.9±0.2		Mean±SEM 2.1±0.2		Mean±SEM 1.8±0.5		Mean±SEM 1.5±0.5		Mean±SEM 0.7±0.08	
Female	3.5	Female	1.9	Female	1.9	Female	1.8	Female	0.6
Female	2.6	Female	2.2	Female	1.8	Female	1.5	Female	1.2
Female	2.1	Female	2.0	Female	1.8	Female	1.6	Female	0.8
Mean±SEM 2.7±0.4		Mean±SEM 2.0±0.08		Mean±SEM 1.9±0.05		Mean±SEM 1.6±0.8		Mean±SEM 0.86±0.1	

Values are shown as mean ± SEM, n=6; The mean distinction is critical at P estimation of < 0.05.

Results demonstrated that rodents pre-treated with Agomelatine before stress had altogether decreased the Ulcer score, contrasted with rodents pre-treated with just 0.5% Xanthan Gum suspension (ulcer control gathering)



FigNo:9 Effect of Agomelatine and its combination on Stomach Volume induced by Stress

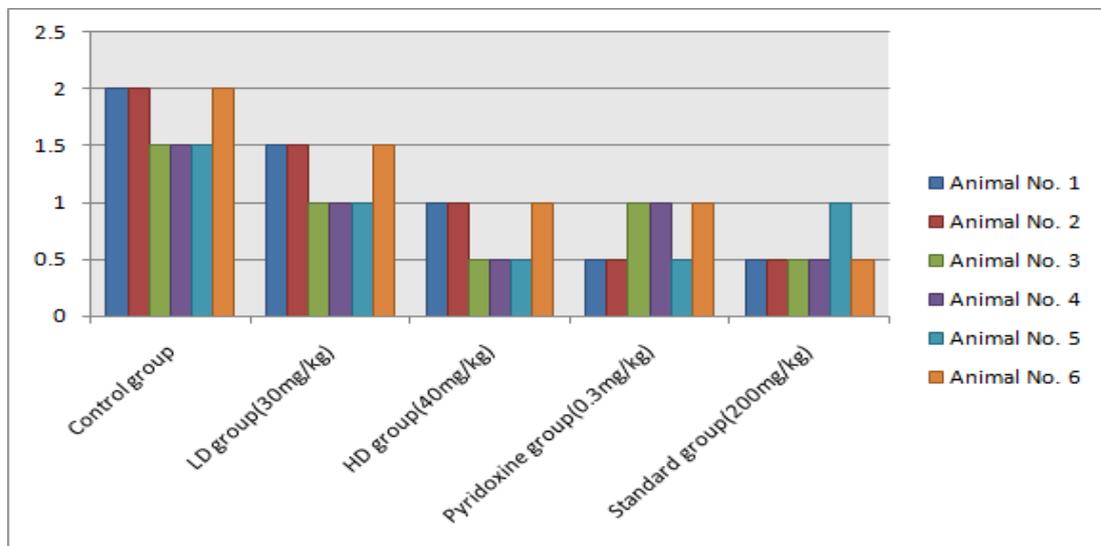
Control Group	LD Group(30 mg/Kg)	HD Group(40 mg/Kg)	Pyridoxine Group(0.3mg/Kg)	Standard Group(200mg/Kg)
				421

Male	2	Male	1.5	Male	1	Male	0.5	Male	0.5
Male	2	Male	1.5	Male	1	Male	0.5	Male	0.5
Male	1.5	Male	1	Male	0.5	Male	1	Male	0.5
Mean±SEM 1.83±0.2		Mean±SEM 1.33±0.16		Mean±SEM 0.83±0.16		Mean±SEM 0.66±0.16		Mean±SEM 0.5±0.00	
Female	1.5	Female	1	Female	0.5	Female	1	Female	0.5
Female	1.5	Female	1	Female	0.5	Female	0.5	Female	1
Female	2.0	Female	1.5	Female	1.0	Female	1	Female	0.5
Mean±SEM 1.66±0.16		Mean±SEM 1.2±0.16		Mean±SEM 0.66±0.16		Mean±SEM 0.83±0.16		Mean±SEM 0.66±0.16	

Table.:9ImpactofAgomelatine,Pyridoxine,andRanitidinepretreatmentonUlcer Scorein Stressactuate stomach ulcer in rodents.

Values are shown as mean ± SEM, n=6; The mean distinction is critical at P estimation of < 0.05.

Results demonstrodented that rodents pre-treated with Agomelatine before stress had essentially diminished the Ulcer score, contrasted with rodents pre-treated with just 0.5% Xanthan Gum suspension (ulcer control gathering).



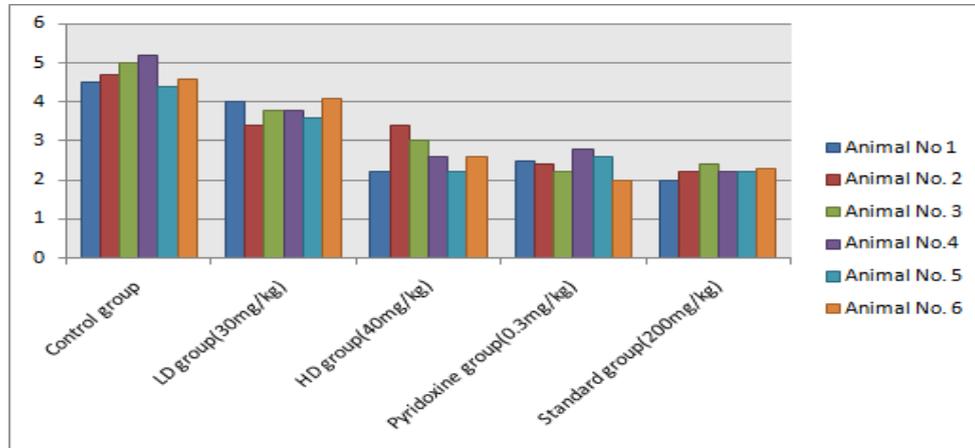
FigNo:10 EffectofAgomelatineandits combinationonUlcer ScoreinducebyStress.

Table.:10ImpactofAgomelatine,Pyridoxine,andRanitidinepretreatmentonUlcer IndexinStressactuate stomach ulcer in rodents.

Control Group		LD Group(30 mg/Kg)		HD Group(40 mg/Kg)		Pyridoxine Group(0.3 mg/Kg)		Standard Group(200mg /Kg)	
Male	4.5	Male	4.0	Male	2.2	Male	2.5	Male	2.0
Male	4.7	Male	3.4	Male	3.4	Male	2.4	Male	2.2
Male	5.0	Male	3.8	Male	3.0	Male	2.2	Male	2.4
Mean±SEM 4.7±0.8		Mean±SEM 3.7±0.5		Mean±SEM 2.8±0.08		Mean±SEM 2.3±0.17		Mean±SEM 2.2±0.11	
Female	5.2	Female	3.8	Female	2.6	Female	2.8	Female	2.2
Female	4.4	Female	3.6	Female	2.2	Female	2.6	Female	2.2
Female	4.6	Female	4.1	Female	2.6	Female	2.0	Female	2.3
Mean±SEM 4.7±0.24		Mean±SEM 3.8±0.17		Mean±SEM 2.4±0.11		Mean±SEM 2.4±0.24		Mean±SEM 2.1±0.08	

Values are shown as mean ± SEM, n=6; The mean distinction is critical at P estimation of < 0.05.

Results indicated that rodents pre-treated with Agomelatine before stress had essentially diminished the Ulcer record, contrasted with rodents pre-treated with just 0.5% Xanthan Gum suspension (ulcer control gathering).



FigNo:1 | Effect of Agomelatine and its combination on Ulcer Index induced by Stress.

Control Group		LD Group(30 mg/Kg)		HD Group(40 mg/Kg)		Pyridoxine Group(0.3 mg/Kg)		Standard Group(200mg /Kg)	
Male	22	Male	18.2	Male	14.3	Male	11.8	Male	10.6
Male	21	Male	18.2	Male	13.7	Male	12.0	Male	9.8

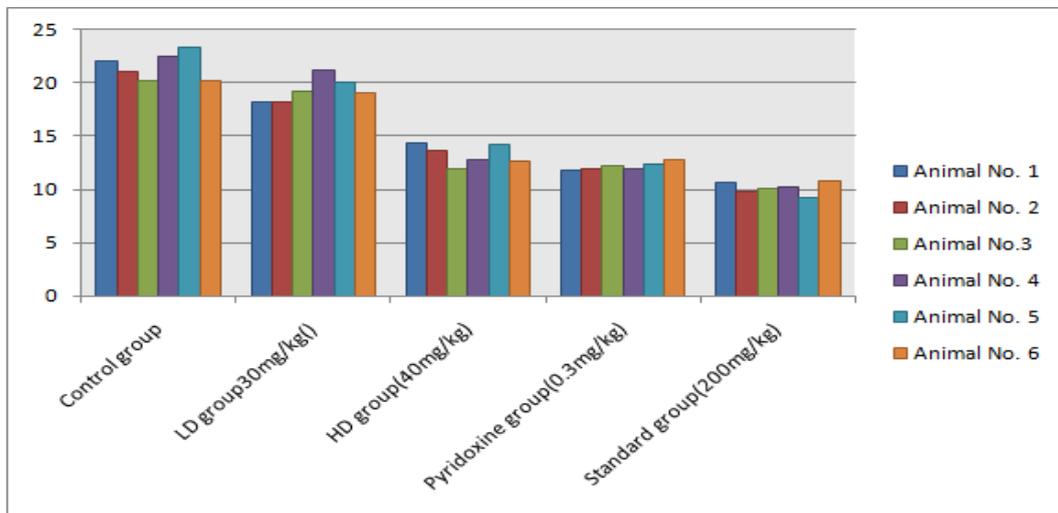
Male	20.2	Male	19.2	Male	12.0	Male	12.2	Male	10.1
Mean±SEM 21.0±0.90		Mean±SEM 18.56±0.88		Mean±SEM 13.36±0.52		Mean±SEM 12.0±0.11		Mean±SEM 10.1±0.14	
Female	22.4	Female	21.2	Female	12.8	Female	11.9	Female	10.2
Female	23.3	Female	20.0	Female	14.2	Female	12.3	Female	9.2
Female	20.2	Female	19.1	Female	12.6	Female	12.8	Female	10.8
Mean±SEM 21.96±0.9		Mean±SEM 20.1±1.5		Mean±SEM 13.2±0.5		Mean±SEM 12.5±0.43		Mean±SEM 10.0±0.29	

Table:-

11 Impact of Agomelatine, Pyridoxine, and Ranitidine pretreatment on free acidity in Stress acute stomach ulcer rodents.

Values are shown as mean ± SEM, n=6; The mean distinction is critical at P estimation of < 0.05.

Results indicated that rodents pre-treated with Agomelatine before stress had essentially diminished the Ulcer record, contrasted with rodents pre-treated with just 0.5% Xanthan Gum suspension (ulcer control gathering).



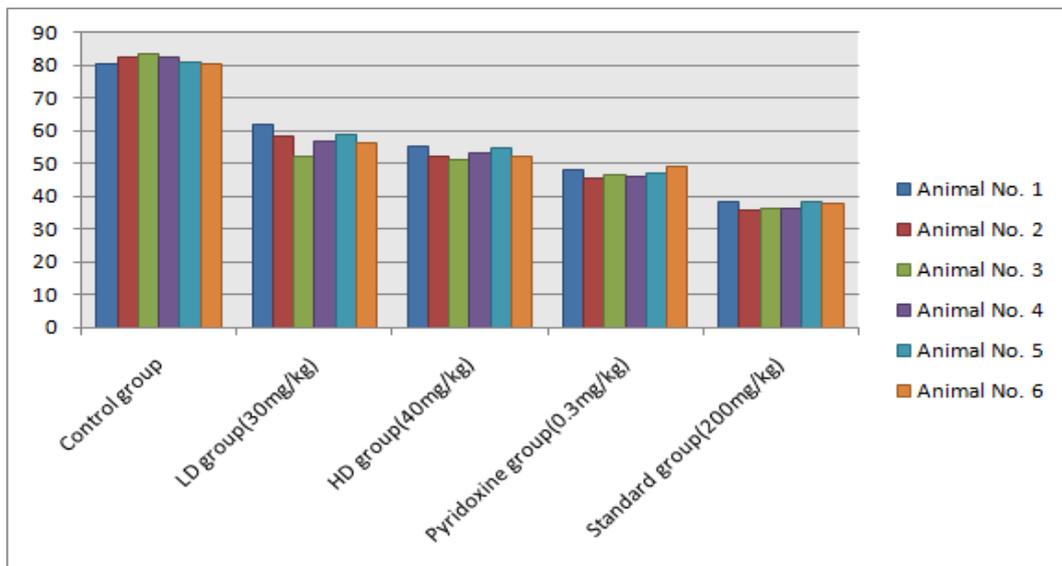
FigNo:12 Effect of Agomelatine and its combination on Free Acidity induced by Stress.

Table:12 Impact of Agomelatine, Pyridoxine, and Ranitidine pretreatment on Total acidity in Stress acute stomach ulcer in rodents

Control Group		LD Group (30mg/Kg)		HD Group (40mg g/Kg)		Pyridoxine Group (0.3mg g/Kg)		Standard Group (200mg/Kg)	
Male	80.2	Male	61.8	Male	55.3	Male	48.2	Male	38.2
Male	82.4	Male	58.2	Male	52.2	Male	45.3	Male	35.9
Male	83.1	Male	52.3	Male	51.1	Male	46.7	Male	36.2
Mean±SEM		Mean±SEM		Mean±SEM		Mean±SEM		Mean±SEM	
81.0±0.87		57.4±1.7		53.1±1.0		46.7±0.83		36.7±0.72	
Female	82.4	Female	56.7	female	53.3	Female	46.2	Female	36.2
Female	80.8	Female	58.9	male	54.9	Female	47.8	Female	38.2
Female	80.3	Female	56.2	male	52.2	Female	48.9	Female	37.8
Mean±SEM		Mean±SEM		an±SEM		Mean±SEM		Mean±SEM	
81.1±0.63		57.1±0.88		53.4±.78		47.6±0.78		37.4±0.61	

Values are shown as mean ± SEM, n=6; The mean distinction is critical at P estimation of < 0.05.

Results showed that rodents pre-treated with Agomelatine before stress, had significantly reduced the Total acidity, compared to rodents pre-treated with only 0.5% Xanthan Gum suspension (ulcer control group).



FigNo:13 Effect of Agomelatine and its combination on Total Acidity induced by Stress

CONCLUSION

Taking everything into account, the consequence of the current examination recommend that Agomelatine (40mg/kg) has Significant gastroprotective impacts against both ethanol and Stress incited stomach ulcer, and furthermore the mix gathering (Agomelatine 40mg/kg + Pyridoxine 0.03mg/kg) indicated more Significant gastroprotective on stomach ulcer.

The defensive impacts against ethanol and Stress incite stomach ulcer were related with lessen free causticity, complete sharpness, stomach volume and ulcer list, when contrasted and Ranitidine Histopathological perception demonstrated that Agomelatine can possibly stifle ulcer at the portion of 40mg/kg, and more potential impact is acquired with Pyridoxine.

Pre or Post-treated rodents with agomelatine indicated that agomelatine fundamentally secure stomach mucosal injury against ethanol-prompted harm. Such assurance was demonstrated to be portion reliant as ascertained by the decrease of ulcer zones in the stomach divider, decrease or hindrance of edema. Be that as it may, further nitty gritty examinations are justified for the utilization of Agomelatine as treatment for stomach ulcer.

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Author contribution

All author participated Equally.

Conflict of interest

None

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None

Ethical Clearance: Taken from Institutional ethical committee.

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