

Antiulcer Activity of Ethanolic Extract of *Psydrax Decoccos*

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ABSTRACT:

The leaves of *Psydrax decoccos*, was made free from the adherent foreign material and air dried. percolated with ethanol, petroleum ether and water in a suxlate extract until the suxlet tube shown transparent liquid. obtained extracts were kept in a desiccator to remove moisture and stored properly until used. The result of the present investigation that the *Psydrax decoccos* which possesses antiulcer activity in aspirin induced, histamine induced. Depression reduces gastric mucosal blood flow and gastric motility which leads to mucosal damage.

KEY WORDS: Extract, Moisture, Gastric Motility, Histamine, Anti-Ulcer, Ethanol, Transparent

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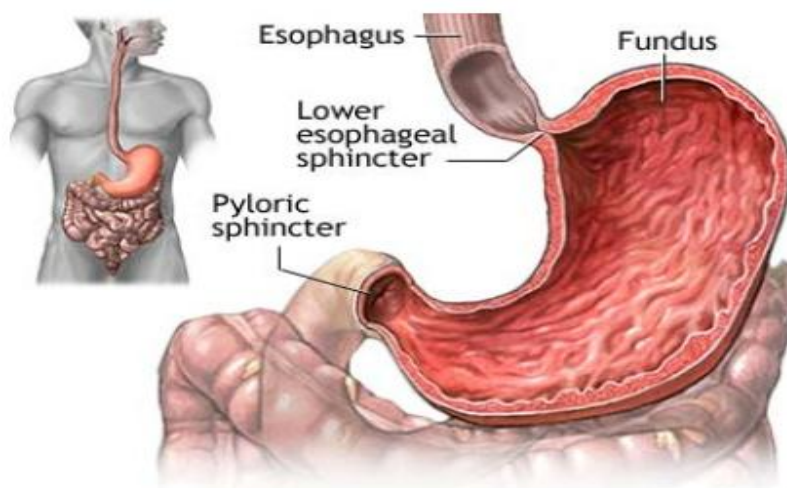
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I. Introduction:

The pathophysiology of peptic ulcer has been centralized on an imbalance between aggressive and protective factors in the stomach such as acid-pepsin secretion, mucosal barrier, mucus secretion, blood flow, cellular regeneration, prostaglandins and epidermal growth factors. Although hospital admissions for uncomplicated peptic ulcers in developed countries had begun decrease, there was a striking rise in admissions for ulcer hemorrhage and perforation among elderly people. This increase has been attributed to the increased use of non-steroidal anti-inflammatory drugs (NSAIDs), alcoholic beverages, cigarettes and *Helicobacter pylori* infections.

The stomach is a portion of the digestive system responsible for breaking down food the lower esophageal sphincter at the top of the stomach regulates food passing from the esophagus into the stomach, and prevents the contents of the stomach from reentering the esophagus.

Hydrochloric Acid: A common misperception is that excess hydrochloric acid, which is secreted in the stomach, is solely responsible for producing ulcers. Patients with duodenal ulcers do tend to have higher-



than-normal levels of hydrochloric acid, but most patients with gastric ulcers have normal or lower-than-normal acid levels. Some stomach acid is important for protecting against *H. pylori*, the bacteria that causes most peptic ulcers. [Note: An exception is ulcers that occur in Zollinger-Ellison syndrome. This is a rare genetic condition in which very high levels of gastrin, a hormone that stimulates the release of hydrochloric acid, are secreted by tumors in the pancreas or duodenum].

Pepsin: Pepsin is an enzyme that breaks down proteins in food. Because the stomach and duodenum are also composed of protein, they are susceptible to the actions of pepsin. Pepsin is, therefore, also an important factor in the formation of ulcers.

The mucus layer: which coats the stomach and duodenum, forms the first line of defense.

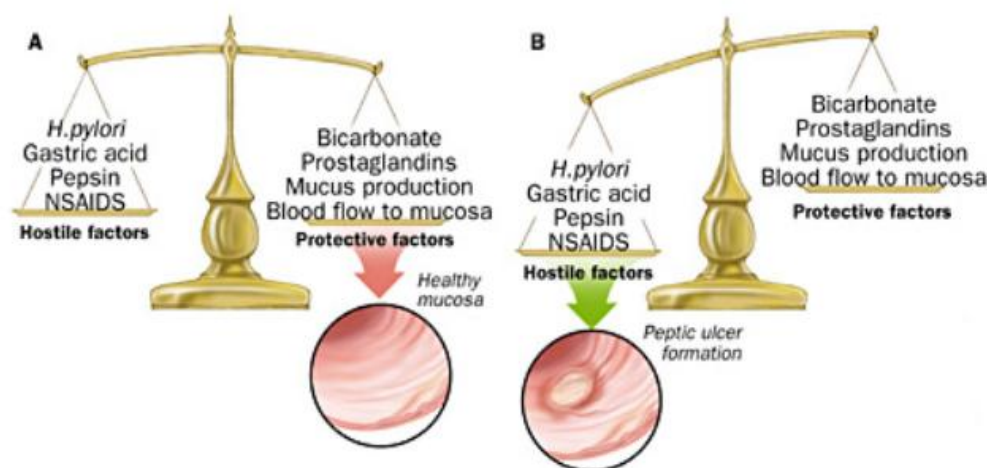
Bicarbonate: which the mucus layer secretes, neutralizes the digestive acids.

Hormone-like substances called prostaglandins help dilate the blood vessels in the stomach, to ensure good blood flow and protect against injury. Prostaglandins are also believed to stimulate bicarbonate and mucus production.

Protective vs. Hostile Factors

“No gastric acid, no peptic ulcer” is a misconception. Excessive gastric acid secretion is only one factor in the pathogenesis of peptic ulcer disease. Decreased mucosal defense against gastric acid is another cause. The integrity of the upper gastrointestinal tract is dependent upon the balance between “hostile” factors such as gastric acid, *H. pylori*, NSAIDs and pepsin, and “protective” factors such as prostaglandins, mucus, bicarbonate, and blood flow to mucosa affecting gastrointestinal mucosa. Injury to gastric and duodenal mucosa develops when deleterious effects of gastric acid overwhelm the defensive properties of the mucosa. Inhibition of endogenous prostaglandin synthesis leads to a decrease in epithelial mucus, bicarbonate secretion, mucosal blood flow, epithelial proliferation, and mucosal resistance to injury. Lower mucosal resistance increases the incidence of injury by endogenous factors such as acid, pepsin, and bile salts as well as exogenous factors such as NSAIDs, ethanol and other noxious agents.

II. Materials And Methodology:



Plant materials: The plant leaves of *Psydrax dicoccos* were collected in the month of August from Guntur area, the plants were authenticated by Dr. Satya madhav dept of Botany, SSN college, Narasaraopet, Andhra Pradesh, India.

Preparation of extracts

The leaves of *Psydrax Dicoccos*, were made free from the adherent foreign material and air dried. This was coarsely powdered and 2kg of each was percolated with ethanol, petroleum ether and water in a Soxhlet extract until the Soxhlet tube showed transparent liquid. After filtered and concentrated under reduced pressure (rotavapor) to yield corresponding extract; the so obtained extracts were kept in a desiccator to remove moisture and stored properly until used.

Pharmacological screening:

Animals used:

Healthy Swiss albino rats (200-250gm) of either sex, housed in animal house of Delves Labs Pvt. Ltd (1675/ro/c/12/CPCSEA Delves Labs Private Limited,) were selected and maintained under standard laboratory conditions of light at 23±2 °C and 55±5% r.h. the animal housing and handling were done in accordance with CPCSEA guidelines. The experiments were conducted as per the norms of institutional animal ethics committee (IAEC). The animals were given standard rat pellet feed and tap water. After one week of acclimatization, rats were randomly selected and grouped into different groups.

CHEMICALS REQUIRED:

Aspirin – 400mg/kg, Histamine – 100mg/kg, NaOH, Topfers reagent, Formalin 10%, CMC 0.5%, Distilled water

EQUIPMENTS:

Microscope, Centrifuge, Animal weighing balance (SONIC), Mechanical stirrer (SONIC), Drug weighing balance (WENSARTM)

DESCRIPTION OF THE PROCEDURES USED:

Preparation of Vehicle:

Dissolve 0.5g of CMC in 100 ml of water to get 0.5% CMC which is used as vehicle

Preparation of Standard solution: Dissolve 0.04g of Omeprazole in 10 ml of Vehicle

Poly herb dose preparation –

Dissolve 400mg/kg and 800mg/kg of Poly Herb in 1 ml of vehicle before dosing

Acute toxicity studies:

Acute toxicity studies carried out according to 420 OECD guidelines, swiss albino rats (150-200 g) were divided into five groups. The rats were fasted for 6 h with only access to water albidum before experimental study. Group I, II, III and IV animals were administered various doses of ethanolic extract of poly herb i.e. 500,1000, 2000, 5000 and 4000 mg/kg. Group V received 0.5% CMC only. All the doses and vehicle were administered by oral route. The animals were observed for 72 h for mortality.

METHODS:

INDUCTION OF ULCER BY ASPIRIN:

Swiss Albino rats weighing 150-200g are taken for this experiment. The rats are administered either the appropriate vehicle or the cytoprotective drug orally 30mins prior to administration of aspirin. This process is done for 6 days and on the last day, the animals are euthanized with chloroform the stomachs are excised, cut along the greater curvature, and gently rinsed under tap water. The stomachs are stretched on a piece of foam core mat and examined under a 3-fold magnifier.

INDUCTION OF ULCER BY HISTAMINE:

Swiss Albino rats weighing 150-200g are taken for this experiment. The rats are administered either the appropriate vehicle or the cytoprotective drug orally 30mins prior to administration of histamine. This process is done for 6 days and on the last day, the animals are euthanized with chloroform the stomachs are excised, cut along the greater curvature, and gently rinsed under tap water. The stomachs are stretched on a piece of foam core mat and examined under a 3-fold magnifier.

EVALUATION PARAMETERS:

Collection of Gastric Juice⁸⁸: The stomach was excised carefully keeping the esophagus closed, opened along the greater curvature and the gastric contents were removed. The gastric contents were collected in plain tubes and centrifuged at 5000 rpm for 5 min; the volume of the supernatant was expressed as ml/100 gm body weight. The mucosa was flushed with saline and observed for gastric lesions using a dissecting microscope, ulcer score was determined.

Ulcer Scoring:

After sacrificing the rat, stomach was removed and opened along the greater curvature, and washed it slowly under running tap water. Put it on the glass slide and observe under 10X magnification for ulcer.

Free acidity and Total acidity:

Centrifuge the gastric contents at 1000 rpm for 10 min, note the volume. Pippete out 1 ml of supernatant liquid and dilute it to 10 ml with distilled water. Note the PH of the solution with the help of PH meter. Titrate the solution against 0.01N NaOH using topfers reagent as an indicator. (It is Dimethyl-amino-azo-benzene with phenolphthalein and used for detection and estimation of hydrochloric acid and total acidity in gastric fluids) Titrate to end point when the solution turns to orange colour. Note the volume of NaOH which corresponds to free acidity. Titrate further till the solution regains its pink colour. Note the total volume of NaOH which corresponds to the total acidity. Acidity (mEq/1/100 g) can be expressed as:

Acidity = mEq/1/100 g

Group I – Control rats(Aspirin +CMC)

Group II – Aspirin induced ulcer rats orally treated with Omeprazole (20 mg/kg b.w)

Group III – Aspirin induced ulcer rats orally treated Poly herb the dose of 400 mg/kg

Group IV – Aspirin induced ulcer rats orally treated with Poly herb 800mg/kg

Statistical analysis of data:

Results were expressed as mean \pm S.E.M. The statistical difference between the groups in the term of the mean rate of wound healing was calculated in terms of ANOVA mean \pm S.E.M. The difference was considered significant if $P < 0.05$. The rats are divided into different groups each comprising of minimum of four rats as detailed below.

III. Result And Discussion:

The Physical Status and Percentage yield of the Extracts:

Percentage yield and physical status of the ethyl alcohol petroleum ether and aqueous extracts of Psydrax decoccos, along with their fractions were summarized in the table:

S.No	EXTRACT	CODE	PHYSICAL STATUS	YIELD (%)
1	Ethanolic extract of leaves of Psydrax decoccos	PDEE	Dark green semi solid	15
2	Petroleum ether extract of leaves Psydrax decoccos	PDPEE	Brown semi-solid	24
3	Aqueous extract of leaves of Psydrax dicoccos	PDAE	Brown semi-solid	17.5

*Yield of extract calculated with respect to the raw materials used and for fraction was with respect to corresponding ethanolic extract used for fractionation Yield of extracts calculated with respect to the raw material used Phytochemical evaluation of Psydrax Dicoccos (PD) The results of preliminary Phytochemical screening of the bioactive fractions were presented in table 5.3 the tests revealed the presence of flavonoids, steroids, Glycosids saponins, phenolic compounds and carbohydrates in PDEE, PDPEE and PDAE

TEST	PDEE	PDPEE	PDAE
Alkaloids			
a) Dragendorffs test	-	-	-
b) Mayers test	-	-	-
c) Wagners test	-	-	-
d) Hagers test	-	-	-
Carbohydrates (Molisch test)	+	+	+
Glycosides	+	-	++
Steroidal (Liebermann-Burchard Reaction)	-	-	+
Saponins (foam Reaction)	++	+	++
Flavonoids(shinoda)	+	+	+
Phenol	++	+	+

Acute toxicity study

No adverse effects and no mortality rate of the animals were observed during the period of 14 days study up to the 2000mg/kg b.w.p.o of the ethanolic extracts of Psydrax dicoccos, The two random doses of 300 and 500 mg/kg b.w. were selected for the hepatoprotective studies.

PHARMACOLOGICAL STUDIES:

IN ASPIRIN INDUCED ULCERS

Effect of Gastric Volume:

Administration of the extract and poly herb significantly decreased the gastric volume in comparison with rats treated with Omeprazole. Comparing the gastric volume and gastric acidity, the gastric volume gets decreased, simultaneously the gastric acidity also decreased significantly.

Effect of Free Acidity and Total Acidity:

The free acidity and total acidity was determined based on the titre values. The free acidity and total acidity of poly herb on albino rats decreased significantly in comparison with the standard group treated with omeprazole.

Ulcer index:

The ulcer index was calculated by taking the mean ulcer score of each groups. Then the mean ulcer score graph was plotted with groups on x-axis and ulcer index on y-axis. The histograms of different groups were then interpolated by comparing the ulcer index of group I with group II, III and IV. It was noticed that the ulcer index of Dose group (Dose-IV) was significantly less when compared to the standard group (Group-II) treated with Omeprazole.

EFFECT OF PSYDRAX DECOCCOS ON GASTRIC VOLUME IN ASPIRIN INDUCED MODEL:

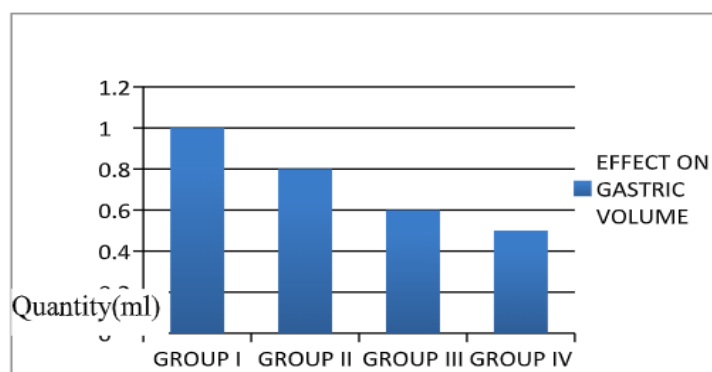
GROUPS	BODY WT. OF RATS	DRUGS GIVEN	GASTRIC VOLUME
GROUPS I	161 ± 1.1	Aspirin + CMC	1.8 ± 0.01
GROUPS II	175 ± 0.5	Omeprazole + Aspirin	1 ± 0.1
GROUPS III	170 ± 0.5	Plant extract (200mg/kg)+ Aspirin	1.1±0.03
GROUPS IV	171 ± 1.1	Plant extract (400mg/kg) + Aspirin	0.83± 0.02

Values are expressed in terms of mean ± SEM of 4 rats (ANOVA)

P values: **< 0.001 - Highly significant * < 0.05 - Significant N S: Non Significant

EFFECT OF POLY HERB ON GASTRIC VOLUME IN ASPIRIN INDUCED MODEL:

GASTRIC VOLUME



Group I :Control received only Aspirin (400 mg/kg) g

Group II : Dose I received plant extract on(200 mg/kg) for 6 days+ Aspirin (400 mg/kg)

Group III : Standard received Omeprazole (20 mg/kg)

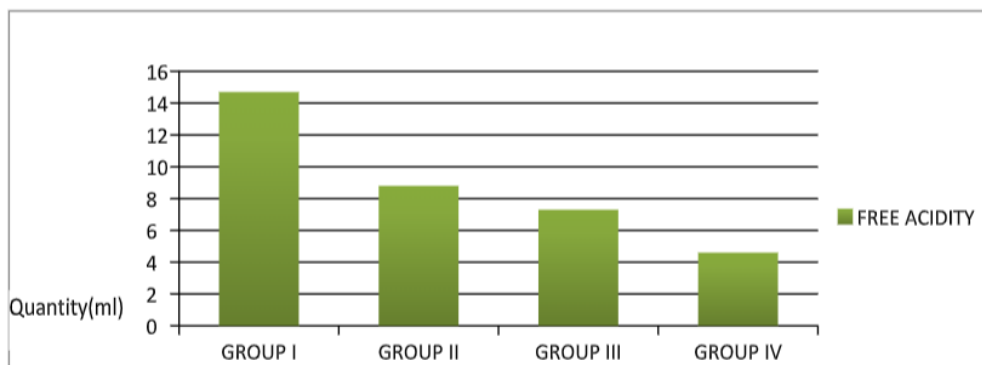
Group IV : Dose II received Plant extract (400 mg/kg) for 6 days+ Aspirin (400 mg/kg)

EFFECT OF PSYDRAX DECOCCOS ON FREE ACIDITY AND TOTAL ACIDITY IN ASPIRIN INDUCED MODEL:

Groups	Body wt. of rats	Drugs given	Free Acidity	Total Acidity
GROUP I	161 ± 1.1	Aspirin + CMC	14.05±0.02	29± 0.01
GROUP II	175 ± 0.5	Omeprazole + Aspirin	9 ± 0.01	16 ± 0.02
GROUP III	170 ± 0.5	poly herb(400mg/kg)+ Aspirin	7 ± 0.04	13± 0.01
GROUP IV	171 ± 1.1	Polyherb(400 and 800mg/kg) + Aspirin	4± 0.08	9± 0.04

Values are expressed in terms of mean ± SEM of 4 rats (ANOVA)

EFFECT OF PSYDRAX DECOCCOS FREE ACIDITY IN ASPIRIN INDUCED



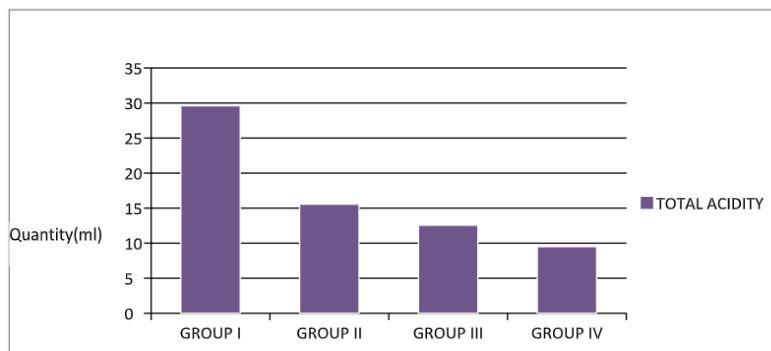
Group I :Control received only Aspirin (400 mg/kg)

Group II : Dose I received Ethanolic extract of plant extract (200 mg/kg) for 6 days+ Aspirin (400 mg/kg)

Group III : Standard received Omeprazole (20 mg/kg)

Group IV : Dose II received plant extract (400 mg/kg) for 6 days+ Aspirin (400 mg/kg)

EFFECT OF PSYDRAX DECOCCOS ON TOTAL ACIDITY IN ASPIRIN INDUCED MODEL:



Group I :Control received only Aspirin (400 mg/kg)

Group II : Dose I received ethanolic extract of plant extract (200 mg/kg) for 6 days+ Aspirin (400 mg/kg)

Group III : Standard received Omeprazole (20 mg/kg)

Group IV : Dose II received Plant extract (400 mg/kg) for 6 days+ Aspirin (400 mg/kg)

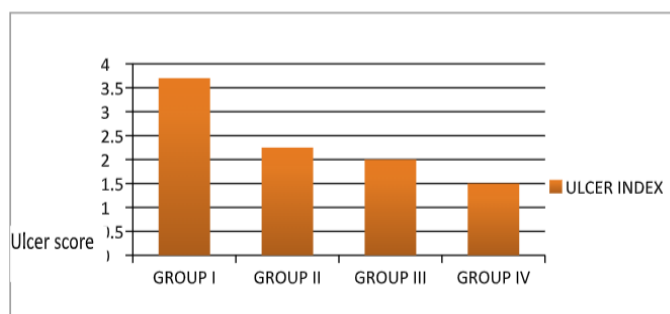
EFFECT OF PSYDRAX DECOCCOS ON ULCER INDEX AND PERCENTAGE

PROTECTION IN ASPIRIN INDUCED ULCER MODEL:

Groups	Body wt of rats	Drugs given	Ulcer index	% Protection
GROUP I	161 ± 1.1	Aspirin + CMC	3.8±0.64	-
GROUP II	175 ±0.5	Omeprazole + Aspirin	2.2±0.6*	97
GROUP III	170 ± 0.5	poly herb(400mg/kg)+aspirin	2±0.5*	98.2
GROUP IV	171 ± 1.1	Poly herb(800mg/kg) + Aspirin	1.5±0.05**	98.8

Values are expressed in terms of mean ± SEM of 4 rats (ANOVA)

EFFECT OF PSYDRAX DECOCCOS ON ULCER INDEX IN ASPIRIN INDUCED ULCER MODEL:



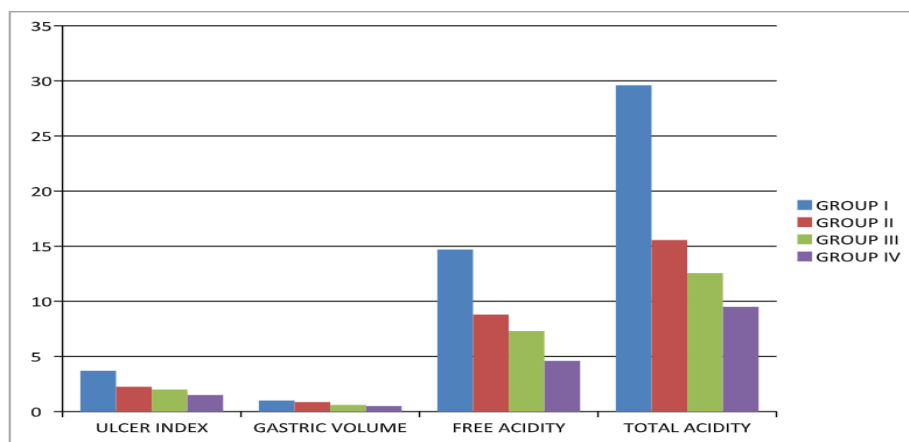
Group I :Control received only Aspirin (400 mg/kg)

Group II : Dose I received plant extract(400 mg/kg) for 6 days+ Aspirin (400 mg/kg)

Group III : Standard received Omeprazole (20 mg/kg)

Group IV : Dose II received Plant extract (400 mg/kg) for 6 days+Aspirin (400 mg/kg)

EFFECT OF PSYDRAX DECOCCOS ON GASTRIC VOLUME FREE ACIDITY TOTAL ACIDITY AND ULCER INDEX IN ASPIRIN INDUCED MODEL:
COMPARISION OF PARAMETERS



Group I :Control received only Aspirin (400 mg/kg)

Group II : Dose I received Plant extract (200 mg/kg) for 6 days+ Aspirin (400 mg/kg)

Group III : Standard received Omeprazole (20 mg/kg)

Group IV : Dose II received plant extract(400 mg/kg) for 6 days+ Aspirin (400 mg/kg)

MACROSCOPICAL VIEW OF RAT STOMACH

After mounting the rat stomach on glass slide and observed in 10x magnification, different scores were noted in each groups. The mean ulcer score represents the ulcer index. The scores on each group were compared, ie group I with group II, III and IV. It was noticed that



Figure : Group I (Aspirin)



Figure : Group II (Omeprazole)

Group II and IV shows similarity in the score as that of group III. Macroscopic appearance of the gastric mucosa in aspirin induced ulcer models:



Figure : Group III (plant extract 200mg/kg)



Figure : Group IV (plant extract 400mg/kg)

IN HISTAMINE INDUCED ULCERS

Effect of Gastric Volume :

Administration of the Plant extract significantly decreased the gastric volume in comparison with rats treated with Omeprazole. Comparing the gastric volume and gastric acidity, the gastric volume gets decreased, simultaneously the gastric acidity also decreased significantly.

Effect of Free Acidity and Total Acidity :

The free acidity and total acidity was determined based on the titre values. The free acidity and total acidity of plant extract on albino rats decreased significantly in comparison with the standard group treated with omeprazole.

Ulcer index :

The ulcer index was calculated by taking the mean ulcer score of each groups. Then the mean ulcer score graph was plotted with groups on x-axis and ulcer index on y-axis. The histograms of different groups were then interpolated by comparing the ulcer index of group I with group II, III and IV. It was noticed that the ulcer index of Dose group (Dose-IV) was significantly less when compared to the standard group (Group- III) treated with Omeprazole.

EFFECT OF PSYDRAX DECOCCOS ON GASTRIC VOLUME IN HISTAMINE INDUCED ULCER MODEL:

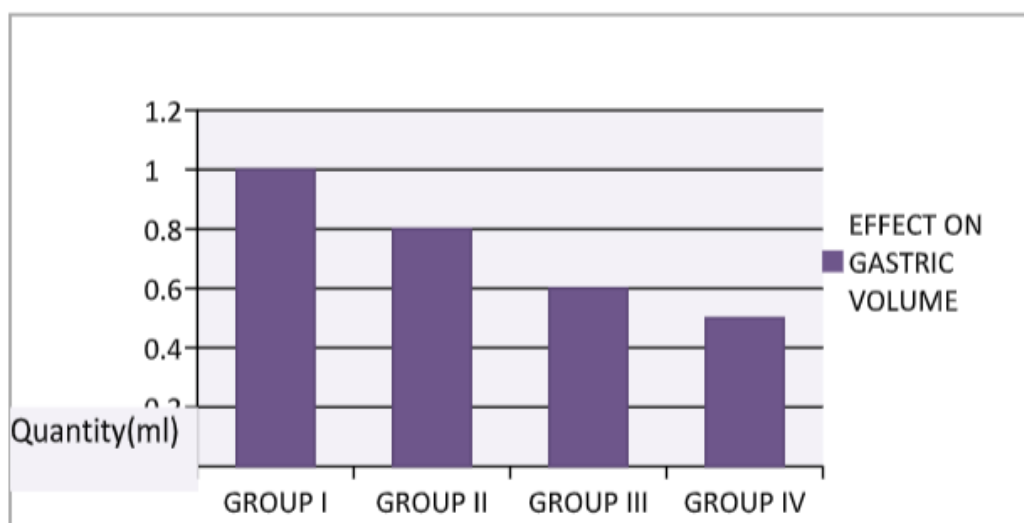
Groups	Body wt. of rats	Drugs given	Gastric volume
GROUP I	176 ± 1.4	Histamine + CMC	1 ± 0.01
GROUP II	163.7 ± 0.5	Omeprazole + Histamine	0.8 ± 0.1
GROUP III	170.7 ± 0.9	Plant extract (200mg/kg) + Histamine	0.6 ± 0.02
GROUP IV	160.2 ± 0.5	Plant extract (400mg/kg) + Histamine	0.5 ± 0.02

Values are expressed in terms of mean ± SEM of 4 rats (ANOVA)

P values: **< 0.001 - Highly significant* < 0.05 - Significant N S: Non Significant

EFFECT OF PSYDRAX DECOCCOS ON GASTRIC VOLUME IN HISTAMINE INDUCED ULCER MODEL:

GASTRIC VOLUME



Group I :Control received only Histamine (100mg/kg)

Group II : Dose I received Plant extract (200 mg/kg) for 6 days+ Histamine(100 mg/kg)

Group III : Standard received Omeprazole (20 mg/kg)

Group IV : Dose II received Plant extract (400 mg/kg) for 6 days+ Histamine (100 mg/kg)

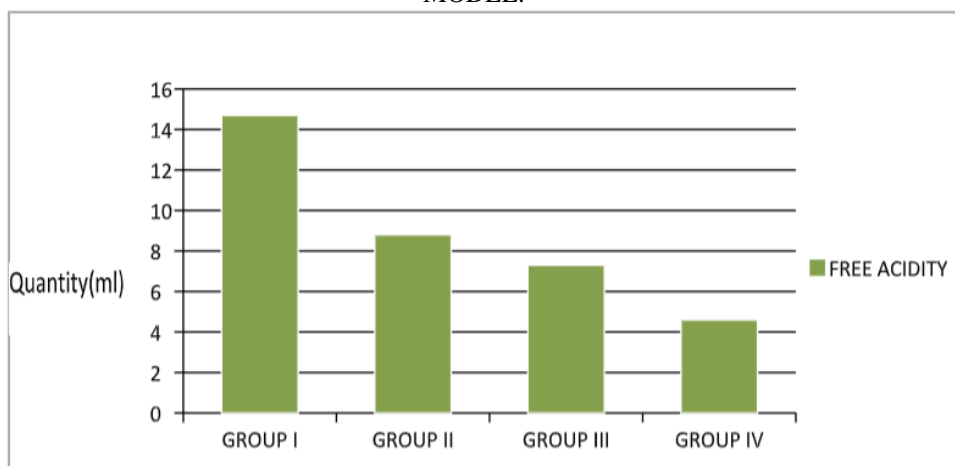
EFFECT OF PSYDRAX DECOCCOS ON FREE ACIDITY AND TOTAL ACIDITY IN HISTAMINE INDUCED ULCER MODEL:

Groups	Body wt. of rats	Drugs given	Free Acidity	Total Acidity
GROUP I	176 ± 1.4	Histamine + CMC	14.8±0.02	29.3±0.02
GROUP II	163.7 ± 0.5	Omeprazole + Histamine	8.8±0.03	16.4±0.04
GROUP III	170.7 ± 0.9	Plant extract (200mg/kg)+Histamine	7.3±0.02	13±0.03

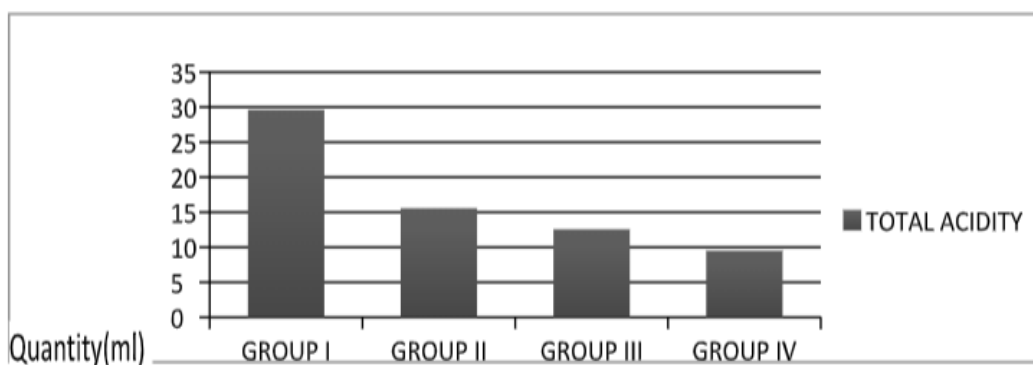
GROUP IV	160.2 ± 0.5	Plant extract(400mg/kg) + Histamine	4.8±0.05	9±0.03
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Values are expressed in terms of mean ± SEM of 4 rats (ANOVA)

EFFECT OF PSYDRAX DECOCCOS ON FREE ACIDITY IN HISTAMINE INDUCED ULCER MODEL:



EFFECT OF PSYDRAX DECOCCOS ON TOTAL ACIDITY IN HISTAMINE INDUCED ULCER



Group I :Control received only Histamine (100 mg/kg)

Group II : Dose I received Plant extract(200 mg/kg) for 6 days+ Histamine (100 mg/kg)

Group III : Standard received Omeprazole (20 mg/kg)

Group IV : Dose II received Plant extract (400 mg/kg) for 6 days+ Histamine (100 mg/kg)

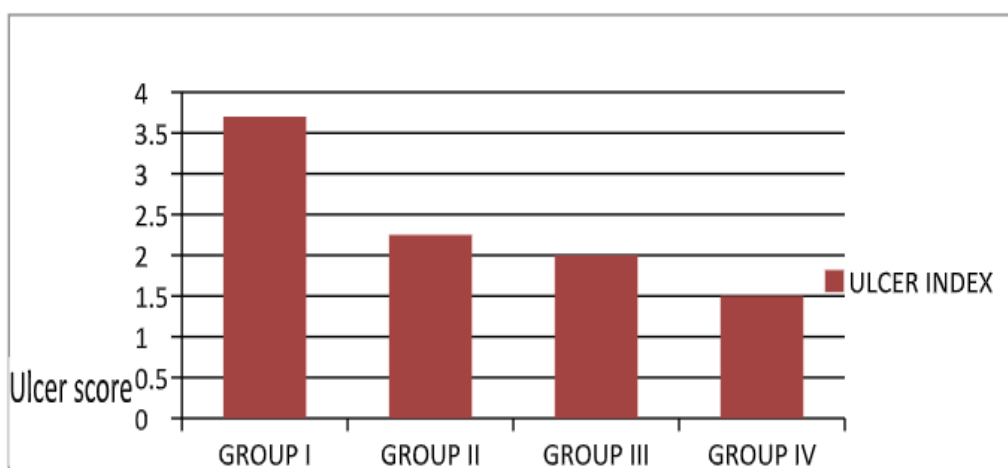
EFFECT OF PSYDRAX DECOCCOS ON ULCER INDEX AND PERCENTAGE OF PROTECTION IN HISTAMINE INDUCED ULCER MODEL:

Groups	Body wt of rats	Drugs given	Ulcer index	% Protection
GROUP I	176 ± 1.4	Histamine + CMC	3.8±0.4	-
GROUP II	163.7 ±0.5	Omeprazole+Histamine	2.2±0.47**	98
GROUP III	170.7 ± 0.9	Plant extract(200mg/kg)+ Histamine	2±0.4*	98.2
GROUP IV	160.2 ± 0.5	Plant extract(400mg/kg)+Histamine	1.5±0.70*	98.8

Values are expressed in terms of mean ± SEM of 4 rats (ANOVA)

EFFECT OF PSYDRAX DECOCCOS ON ULCER INDEX IN HISTAMINE INDUCED

ULCER MODEL:



Group I :Control received only Histamine (100 mg/kg)

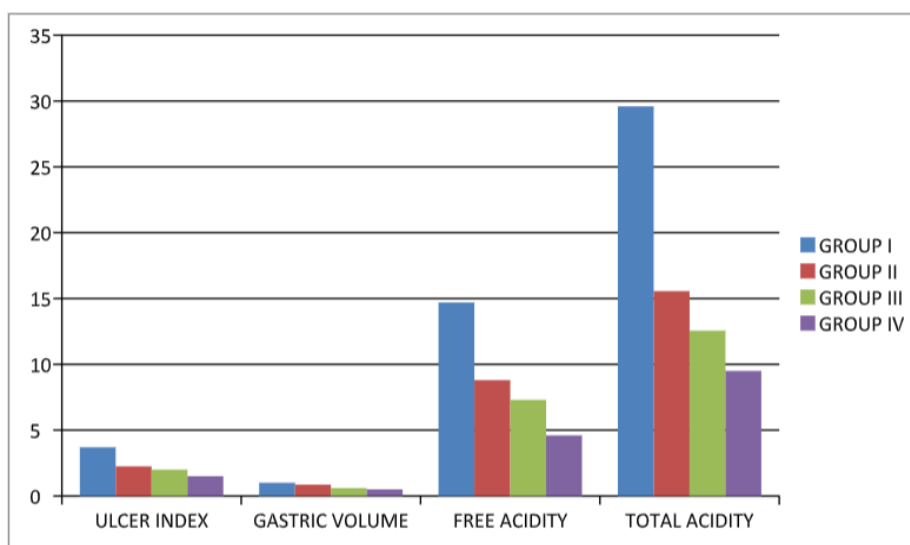
Group II : Dose I received Plant extract(200 mg/kg) for 6 days+ Histamine (100 mg/kg)

Group III : Standard received Omeprazole (20 mg/kg)

Group IV : Dose II received Plant extract (400 mg/kg) for 6 days+ Histamine (100 mg/kg)

EFFECT OF PSYDRAX DECOCCOS ON GASTRIC VOLUME FREE ACIDITY TOTAL ACIDITY ULCER INDEX IN HISTAMINE INDUCED ULCER MODEL:

COMPARISION OF PARAMETERS:



Group I :Control received only Histamine (100 mg/kg)

Group II : Dose I received Plant extract(200 mg/kg) for 6 days+ Histamine (100 mg/kg)

Group III : Standard received Omeprazole (20 mg/kg)

Group IV : Dose II received Plant extract(400 mg/kg) for 6 days+ Histamine(100 mg/kg)

Macroscopic appearance of the gastric mucosa in histamine induced ulcer models:



Figure: Group II (Omeprazole)



Figure: Group I (Histamine)



Figure : Group III (plant extract 200mg/kg)
400mg/kg)



Figure : Group IV (plant extract 400mg/kg)

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