Gastroprotective effect of leaves of *Breyniavitis-Idaea*

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**ABSTRACT**
Due to the lure backs of synthetic drugs that are being used medical field has turned over to the traditional medicine which are devoid of side effects and major adverse effects. So that Herbal drugs were seen as probable replacements for the handling of PUD without showing side effects and equaling the treatment efficacy. The literature review on investigations of antulcer activity of various plant drug, the present investigation was carried out to investigate the antulcer potential, chemical constituents present in the methanol extract of traditional plant Breyniavitis-idaea. Gastric ulcers in experimental animals were brought by four different models like Ethanol(Alcohol) induced, NSIDS (Indomethacin) induced, Pylorus ligation method and Cold resistant stress induced method by comparing with the standard drug namely omeprazole (20mg/kg) which exhibited the dose dependent capacity of the extract (125mg/kg, 250mg/kg, 500mg/kg) and also the biochemical parameters like ALP, GSH, pH and Gastric volume contents were estimated in all the selected groups (Design of Experiment). The results obtained from the study has helped to identify that 500mg/kg of plant extract has gastroprotective effect in all the chosen models in comparison to the omeprazole (20mg/kg) standard drug. Owing to the prevalence of different phytoconstituents like poly phenols and flavonoids shown the dose dependent potent gastroprotective activity.

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**INTRODUCTION**

PUD (Peptic Ulcer Disease) distresses most of the people in the world and disabling their daily activities. It is noted as one the commonest and stubborn diseases that occur in people and affect their lives (Antonio et al., 2004). There are various factors involved to cause the disease such as oxidative stress, chronic and excessive smoking, malnutrition and due to chronic use drugs like NSAID’s and steroids. The imbalances in the offensive and defensive factors like HCl, enzymes, H. Pylori and Mucin, prostaglandins NO2 and carbonates and bicarbonates act as common factors in causing the PUD (Baggio et al., 2003; Chiang et al., 2005; Cho and Ogle, 1979; Cho et al., 1976).

One of the major setbacks of the PUD treatment is the incidence and development of drug tolerance and others being relapse of disease, noting of side effects on clinical observation after treatment.
Table 1: Gastroprotective Effect of MEBV in experimental animals

| Gastroprotective Effect of MEBV in experimental animals | Cold-Restraint (I) | Pylorus ligation (%) | Indomethacin (%) | Ethanol model (%) |
|------------------------------------------------------|-------------------|---------------------|-----------------|-----------------|
| NA | No inhibition | 11.27 | 33.85 | 48.73 | 42.42 |
| UI | No ulcerous lesions | 5.69+ | 12.33 | 7.76 | 18.60 |
| UI | No ulcerous lesions | 4.62+ | 7.65 | 4.01 | 10.35 |
| UI | No ulcerous lesions | 2.96+ | 4.92 | 3.04 | 8.04 |
| UI | No ulcerous lesions | 2.33+ | 4.15 | 2.48 | 4.57 |

(|%I=Percentage of inhibition, UI=Ulcer index|
Data are situated epitomized as mean ± S.E.M, ANOVA shadowed by Dunnett’s multiple comparison test. *P<0.01 and **P<0.001 as equated to control (n=6 in each group).

Table 2: Effect of MEBV on GSH (µg/mg protein)

| Group | Alcohol persuaded gastric ulcer model | NSAIDS persuaded gastric ulcer model | Pylorus ligated ulcer model | Cold-restraint stress persuaded ulcer model |
|-------|--------------------------------------|-------------------------------------|-----------------------------|--------------------------------------------|
| I     | 2.87 ± 0.330                         | 3.05 ± 0.221                        | 2.75 ± 0.222                | 2.94 ± 0.285                              |
| II    | 0.97 ± 0.270                         | 0.92 ± 0.272                        | 0.81 ± 0.26                 | 0.94 ± 0.352                              |
| III   | 1.31 ± 0.321*                        | 1.35 ± 0.171*                       | 1.35 ± 0.222                | 1.54 ± 0.172*                             |
| IV    | 1.37 ± 0.220**                       | 1.54 ± 0.122**                      | 1.52 ± 0.372**              | 1.65 ± 0.371**                            |
| V     | 1.65 ± 0.890**                       | 1.69 ± 0.220**                      | 1.74 ± 0.332**              | 1.82 ± 0.330**                            |
| VI    | 1.77 ± 0.331**                       | 1.76 ± 0.240**                      | 1.78 ± 0.242**              | 1.87 ± 0.220**                            |

All the numbers set were expressed as mean ± SEM.*P< 0.01 when compared with control group.P< 0.01 when compared with normal group.

These drawbacks of synthetic drugs make the efficacy of drugs quite arguable. This triggered the scope for search and development of newer drugs that treat PUD. Herbal drugs were seen as potential alternatives for the treatment of PUD without showing side effects and equaling the treatment efficacy (Danielsson et al., 2003; Fellenius et al., 1981). Following the literature review on investigations of antiulcer activity of various plant drug, the current study was used to explore the antiulcer potential, chemical elements present in the methanol extract of leaves of Breynia vitis-idaea, (Family: Poaceae) and the same is being reported here (Flemstrom et al., 1982).

**MATERIALS AND METHODS**

**Collection and Authentication of the plant material**

The plant part of Breyniavitis-idaea (Family: Phyllanthaceae) leaves were obtained from Chittoor District, validated by Dr. Madhava Chetty, Asst Profes-
Table 3: Effect of MEBV on ALP (IU/L) of gastric ulcer persuaded models

| Group | Alcohol persuaded gastric ulcer model | Indomethacin persuaded gastric ulcer model | Pylorus ligation stress persuaded Gastric ulcer model |
|-------|--------------------------------------|------------------------------------------|---------------------------------------------------|
| I     | 68.22 ± 2.54                         | 59.24 ± 2.21                             | 70.29 ± 2.32                                      |
| II    | 179.54 ± 2.33                        | 188.19 ± 3.42                            | 195.67 ± 3.38                                     |
| III   | 123.64 ± 2.43*                       | 120.14 ± 3.52*                           | 130.41 ± 3.22*                                   |
| IV    | 113.35 ± 2.58**                      | 115.22 ± 2.32**                          | 116.52 ± 2.41**                                  |
| V     | 82.45 ± 1.48**                       | 86.33 ± 1.24**                           | 85.22 ± 1.57**                                   |
| VI    | 79.54 ± 1.12**                       | 83.21 ± 1.54**                           | 82.12 ± 1.33**                                   |

All values in the statistics set were expressed as mean ± S.E.M. *P<0.01 when equated with control group. P<0.01 when compared with normal set.

Table 4: Effect of MEBV on Gastric volume (ml/100g)

| Group | Alcohol made gastric ulcer model | NSAIDS made gastric ulcer model | Pylorus ligation made ulcer model | Cold-restraint stress made Gastric ulcer model |
|-------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| I     | 0.38 ± 0.03                     | 0.36 ± 0.02                     | 0.45 ± 0.02                     | 0.57 ± 0.02                     |
| II    | 2.66 ± 0.05                     | 2.39 ± 0.01                     | 2.47 ± 0.03                     | 2.57 ± 0.05                     |
| III   | 1.12 ± 0.84*                    | 1.02 ± 0.03*                    | 1.17 ± 0.02*                    | 1.22 ± 0.03*                    |
| IV    | 0.93 ± 0.87**                   | 0.91 ± 0.05**                   | 0.99 ± 0.05**                   | 0.92 ± 0.05**                   |
| V     | 0.68 ± 0.91**                   | 0.64 ± 0.05**                   | 0.69 ± 0.03**                   | 0.69 ± 0.02**                   |
| VI    | 0.54 ± 0.05**                   | 0.54 ± 0.03**                   | 0.57 ± 0.05**                   | 0.58 ± 0.05**                   |

All values in the data set were articulated as mean ± S.E.M. *P<0.01 when equated with control group. P<0.01 when equated with normal group.

Table 5: Effect of MEBV on pH of gastric contents

| Group | Alcohol persuaded gastric ulcer model | Indomethacin persuaded gastric ulcer model | Pylorus ligation stress persuaded Gastric ulcer model |
|-------|--------------------------------------|------------------------------------------|---------------------------------------------------|
| I     | 5.11 ± 0.19                          | 5.60 ± 0.33                              | 5.61 ± 0.41                                      |
| II    | 1.49 ± 0.33                          | 1.52 ± 0.21                              | 1.62 ± 0.22                                      |
| III   | 3.74 ± 0.12*                         | 3.90 ± 0.17*                            | 3.58 ± 0.33*                                    |
| IV    | 4.46 ± 0.59**                        | 4.50 ± 0.14**                           | 4.48 ± 0.37**                                   |
| V     | 4.84 ± 0.31**                        | 4.87 ± 0.22**                           | 4.95 ± 0.19**                                   |
| VI    | 5.22 ± 0.29**                        | 5.17 ± 0.41**                           | 5.22 ± 0.33**                                   |

All values in the data set were voiced as mean ± S.E.M. *P<0.01 when equated with control group. P<0.01 when equated with normal group.

Animals Used

Albino rats of either sex weighing 150–200g were kept in a 12 h light or dark cycle at a constant moderate thermal condition at 25°C with free access to libitum.

Acute toxicity study

Acute toxic dose of methanol extract of leaves of Breynia vitis-idaea., (Family: Poaceae) were determined following OECD guideline no. 423 (Acute Toxic Class Method). Found that the test extracts weren’t deadly or toxic to the experimental animals was smooth at 2000mg/kg dose.

Ethical clearance was approved by IAEC (Institutional Animal Ethical Clearance) Reg No: SVCOP/IAEC/007/2016-17.
Design of Treatment

Group I - control (1% W/V CMC, 10 ml/kg b.w) p.o
Group II - Negative control (1% W/V CMC, 10 ml/kg b.w) p.o
Group III - MEBV (125 mg/kg b.w) p.o
Group IV - MEBV (250 mg/kg b.w) p.o
Group V - MEBV (500 mg/kg b.w) p.o
Group VI - Std. Omeprazole (20 mg/kg b.w) p.o

Ulcer inducing models

Ethanol Induced Gastric Ulcer
8 ml/kg of alcohol was administered to all the assemblies of rats excluding the assembly 1 for which is well thought-out as normal healthy group (Grijalva and Novin, 1990; Gupta et al., 1985). The ulcer catalog for to each rat was taken as the mean ulcer score (Hase and Moss, 1973).

NSAIDS (Indomethacin) Induced Gastric Ulcer
Ulcers lesions in the stomachs of experimental animals were induced with the help of indomethacin (40 mg/kg p.o) administered to all groups after fasting for 24 h (Hoogerwerf and Pasricha, 2001).

Pyloric Ligation Induced Gastric Ulcer
This procedure was not performed on normal healthy group (group 1). After 4 h from surgery, animals were forfeited through cervical dislodgment and score of ulcers was noted on the dissevered stomachs (Kahraman et al., 2003).

Cold-Restraint Stress-Induced Ulcers
Followed as per (Manonmani et al., 1995).

Measurement of ulcer index
Ulcer index (UI), and percentage of inhibition of ulcer lesions (%I) were calculated as described in (Pillai and Santhakumari, 1984).

\[
%I = \left( \frac{USc - USt}{USc} \right) \times 100
\]

Statistical analysis
All the numbers were articulated as mean ± standard error mean (SEM). Implication of variances among the group was calculated by using ANOVA.

RESULTS AND DISCUSSION

The methanol extracts of leaves of Breynia vitis-idaea showed a certainly defensive effects contrary to ulcers persuaded by alcohol, NSAIDS (indomethacin), Pylorus ligation and cold restraint models. The release of free radicles is the mechanism seen in ethanol induced ulcers which can be further supported by its improved activity in pylorus ligated method (Sasajima et al., 1978). The extract valor has also had an asset to rise prostaglandins thereby constructing a mucosal layer for shielding the ulcer from any direct exposure to the acid which is apparent from indomethacin induced gastric ulceration model (Shah et al., 1997). The NSAID drug is a COX inhibitor which disrupts the membrane integrity and causing rupture in the flow of blood. The extract might have helped in production of endogenous prostaglandins for protecting the ulcers (Shay et al., 1945; Singh and Majumdar, 1999; Szabo et al., 1985). Gastric ulceration made by cold restraint stress is undoubtedly facilitated by the upsurge in gastric motility, degranulation of mast cells, decreased gastric mucosal blood, lowering in the prostaglandin synthesis and excretion of glycoproteins in the mucus (Taira et al., 2005; Valle, 2005; Warrier et al., 1995; Weiner, 1996). Any of the above factors could have played an important role in the formation of ulcers. Finally, the extract was proven to have antioxidant activity and it is proven successful in thwarting the ulcers produced due to the physical strain or stress which produces reactive oxygen species detrimental to the stomach lining (Yamamoto et al., 1992).

CONCLUSIONS

MEBV has exhibited dose reliant inhibition in ethanol induced stomach ulcer lesions and stimulate the secretion of prostaglandins or possess prostaglandins like-substances reveals that the as a potent inhibitor of stomach mucosal abrasions caused by ethanol, indomethacin, pylorus ligation and cold-restraint stress in rats. Further, our results support the ethnopharmacological claims of Breynia vitis-idaea as potent anti-ulcer agent. Etiologies of ulcers produced in different ulcer models are different. The study concluded that MEBV and its dynamic constituents may emerge as more effective healing agent to counter gastric ulcer.

Conflict of interest

Authors affirm that No interest of conflicts.

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