

Exploring The Therapeutic Potential Of *Manilkara Zapota* Seed Extract: A Comprehensive Study On Phytochemical Composition And Anti-Ulcer Pharmacology

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Abstract

Medicinal plants have historically served as significant reservoirs of therapeutic agents worldwide. India possesses an extensive repository of traditional medicinal flora, coupled with distinct plant and animal ecosystems. Contemporary advancements in comprehending the pathogenesis of peptic ulcers have propelled the pursuit of novel and enhanced drug therapies. In this particular investigation, the anti-ulcer potential of the seeds of *Manilkara zapota*, an indigenous medicinal plant, was rigorously assessed.

Manilkara zapota seeds emanate from a deciduous tree within the *Sapotaceae* botanical family. These seeds were meticulously subjected to a comprehensive pharmacognostic evaluation. A multifaceted approach encompassing macroscopic, microscopic, physicochemical, and phytochemical methodologies was employed to discern defining characteristics for the identification and standardization of both the intact and pulverized forms of *Manilkara zapota* seed material. Such analytical endeavors served to effectively distinguish it from other botanical constituents.

The finely ground plant material was subjected to solvent extraction through a Soxhlet apparatus, utilizing two distinct solvent systems, namely ethyl acetate and methanol, following prior defatting with petroleum ether.

Subsequent phytochemical analyses of the extracts revealed the presence of a diverse array of bioactive compounds, including carbohydrates, glycosides, tannins, flavonoids, polyphenols, phytosterols, and amino acids, among others. The authenticity of these findings was corroborated through thin-layer chromatography (TLC) analysis.

The quantitative assessment of total phenolic and flavonoid content in the plant extracts was

expressed in terms of gallic acid equivalents and quercetin equivalents, respectively. It was observed that the ethyl acetate extract exhibited a total phenolic content of 39.02, whereas the methanolic extract displayed a content of 46.25.

To evaluate the antioxidative potential, the in-vitro antioxidant activity was gauged using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay. Notably, the methanolic extract showcased heightened antioxidant efficacy with an inhibition rate of 88.08%, surpassing the ethyl acetate extract's rate of 76.53%. This outcome was found to be comparable to the antioxidant activity of the standard ascorbic acid, exhibiting a 94.60% inhibition rate against free radicals at a concentration of 100 µg/ml.

Furthermore, both the ethyl acetate and methanolic extracts underwent scrutiny for their anti-ulcer potential using an ethanol-induced ulcer model in albino rats (Wistar strains). The reference standard employed was ranitidine. Notably, the ethyl acetate extract exhibited a superior percentage of inhibition against ulcer formation, achieving an impressive rate of 86.98%, while the methanolic extract demonstrated a rate of 69.66%.

In summation, this study underscores the significant potential of the ethyl acetate extract of *Manilkara zapota* seeds as a prospective anti-ulcer agent. The meticulous analysis of the plant material lends credibility to its identification and differentiation from other botanical counterparts. While the findings are promising, further exploration through rigorous clinical investigations is imperative to ascertain the full spectrum of therapeutic efficacy and safety profile of these extracts.

Keywords: *Manilkara Zapota Seeds* Standardization, Anti-oxidant activity, Ethanol induced Ulcer.

INTRODUCTION:

Multicellular Organism have A system of organ in the gastrointestinal (GI) tract that enable them to ingest, digest, and Absorb nutrients from food, and eventually eliminate unwanted material. These essential Function, which for the most part occurs involuntarily, are Facilitated by the presence of a well organized nervous system. The GI tract also has the capacity to provide conscious awareness (sensation of pain) that alerts an organism of impending tissue damage which could hamper these vital physiological function. Normally, it involves interplay between immune, peripheral and central nervous system.

Ulcer is an open sore on an external or internal surface of the body, caused by a break in the skin or mucous membrane which fails to heal. Ulcers range from small, painful sores in the mouth to bedsores and serious lesions of the stomach or intestine.

The Pathophysiology of peptic ulcer disease involves imbalance between Aggressive factors (Acid, pepsin And *Halobacter pylori*) And defensive Factors (musin, prostaglandins, bicarbonate, nitric acid and growth factors.). Peptic ulcer are once believed to be caused by spicy food and stress And other factors results from an imbalance between factors that can damage the gastroduodenal mucosal lining and defence mechanism that normally limit the injury. Aggressive factors include gastric juice (including hydrochloric Acid, pepsin, and bile salts refluxed from the duodenum), *H pylori* And NSAIDs (non steroids anti-inflammatory drugs). Diseases like Zollinger – Ellison syndrome, emotional stress, Alcohol abuse and smoking are the principle etiological factors associated with peptic ulcer. bacterium *Halobacter pylori* resides in the antrum but over time migrates towards the more proximal segments of the stomach.

Manilkara Zapota seeds

In the present study we have selected a plant name *Manilkara Zapota* seeds belonging in family *Sapotaceae*. The manilkara zapota plant contain flavonoids, alkaloids.

Sapodilla is a medium to large sized tree with dense and almost round canopy formed by profuse branching system. Initially the growth of these trees is slow but after many years, may reach up to 20-30 metres in height. All tree parts exude out milky latex known as “chicle”.

Roots: Sapodilla roots show shallow-root system with a major portion of roots present within the top 75 cm of soil and about 66% of the moisture extracted from the soil is in the first 75 cm.

Leaves: The leaves are evergreen and spirally arranged (7-12×2-4cm in size), pinkish brown when young and turns light-dark green at maturity. Secondary veins make a wide angle with the midrib.

Flowers: Flowers are small, bisexual, bell-shaped (10 mm in diameter), borne singly or in clusters in the axils of leaves near the branch tips.

Fruit: The fruit of sapodilla is a brown coloured berry, nearly round and varies from 5-10 cm in width. The unripe fruit is hard and coarse whereas it becomes soft and juicy on maturity.

Seeds: Some Sapodilla fruits are seedless but normally they produce 3-12 seeds per fruit. They are hard and brown or black in colour with one white margin. The seeds contain some phytochemicals like saponin, saponin, achras saponin and the bittersapontin. Hydrocyanic acid is also present in seeds, so should be removed before eating the fruit.

MATERIALS AND METHOD

Collection of Plant Material:

The seeds of *Manilkara Zapota* were collected from local region of Nanded city and plant was authenticated at department of Botany and horticulture, Yeshwant Mahavidyalaya, Nanded. Collection, authentication, identification, processing and storage have been done according to standard procedure for the plant material. (The Indian Pharmacopoeia, 2007).

Extraction of plant material

Selection of Solvent.

On the basis of nature of phytochemical present in drug and literature review, solvents were selected for the extraction of the seeds of *Manilkara Zapotaseeds* like Petroleum ether, Ethyl Acetate and Methanol.

After completion of extraction extract was cooled and dried and stored in air tight container and kept in desiccator till use.

Preliminary Phytochemical Evaluation

Qualitative chemical tests were carried out for all three extracts to identify the presence of various chemical constituents and presented.

TLC fingerprinting:

All the extracts of selected plant material were subjected to TLC studies using various solvent systems to determine the presence of various Phytoconstituents. The R_f of observed compounds were noted for all extracts. The characteristic fingerprint of the various chemical constituents in each extract under UV light and after derivatisation with suitable reagents was recorded.

Preliminary phytochemical screening revealed the presence of flavonoids, Tannins, glycoside, amino acid. Compounds of varying polarity in the extracts well separated using various solvent systems on TLC. R_f value of the separated compounds were recorded.

Pharmacological Screening of plant extracts:

In-vitro studies:-

In-vitro study of seeds of *Manilkara zapotawas* done in which following study was carried out which includes,

- In-vitro Anti-oxidant studies.

In-vitro Anti-oxidant studies.

In-vitro Anti-oxidant study of seeds of *Manilkara zapotawas* carried out by DPPH (2, 2-dipheny 1, 1-picrylhydrazyl) radical scavenging activity as per the standard reference procedure.

In-Vivo Studies:

Wistar Rats were kept under controlled conditions of temperature ($22 \pm 2^\circ\text{C}$). All animals were given standard diet and water regularly. These wistar rats of either sex weighing between 160 to 180 gm were used in the present study. The experimental animals were maintained under standard laboratory conditions. Animals were maintained under 12 h light/dark cycles and controlled temperature ($24 \pm 2^\circ\text{C}$) and fed with commercial pellet diet and water ad libitum. All animals were acclimatized to the laboratory environment for at least one week before the commencement of experiment.

For present study animal model used was Ethanol induced anti-ulcer activity.

Ethanol induced ulcer.

The following Six group were made for the antiulcer study.

Group I : Animals were given 0.5 % of DMSO/ Saline water orally.

Group II : Animals were given standard drug (Ranitidine 20mg/kg)

Group III : Animals were given 100mg/kg dose of Ethyl Acetate extract of *Manilkara zapota seeds Extract* (MZEA100mg/kg oral).

Group IV : Animal were receiving 200 mg/kg dose of Ethyl Acetate extract of *Manilkara Zapota seeds extract* (MZEA200mg/kg oral).

Group V : Animals were receiving 100mg/kg dose of Methanolic extract of *Manilkara Zapota seeds Extract* (MZME100mg/kg oral)

Group VI : Animals were received 200mg/kg dose of Methanolic extract of *Manilkara Zapota Seeds extract* (MZME 200mg/kg oral)

Procedure:

- Male Wistar rats weighing 250–300 g were deprived of food 18 h prior to the experiment but was allowed free access to water.
- The rats were administered the vehicle intragastrally 30 min prior to administration of 1 ml absolute ethanol. Untreated animals were included as controls.
- One hour after administration of ethanol, the animals was euthanized with CO₂, the stomachs was excised, cut along the greater curvature, and rinsed with running water.
- A circular full thickness was, about 13 mm in diameter, is cut with a cork borer from each lobe of the fundus just below the ridge dividing the glandular from the non-glandular portion of the stomach.
- The stomachs were stretched on a piece of foam core mat, mucosal site up. The subjective scores of the treated tissues was recorded; the graded response is reflecting the least (0) to most (3) damage.
- A Plexiglas template (19 × 14 × 0.3 cm), burnished on one side with emery cloth, and with four rows with six holes 13 mm in diameter is placed on a sheet of clear glass, burnished side up, and bound to the glass with photographic tape along the periphery. The excised pairs of tissue

from each stomach was placed into the holes of the template. Pairs of tissue from each stomach was examined to minimize sampling errors.

- The template is positioned on a rectangular central open was of an Aristo Model T-16 cold cathode trans illuminator (38 × 38 cm) containing a W-45 blue-white lamp. A camera is mounted on a copy stand directly above the template. Photographs was taken, the film processed in a standard manner and a contact sheet is made from the negatives.

% Ulcer index = (Ulceration area / Total stomach area)

OBSERVATIONS AND RESULTS

Pharmacognostic evaluation of *Manilkara Zapota Seed*

Table: Physical parameter of *Manilkara zapota* seeds

Physical parameters	%(w/w)
Loss on drying	11.25
Total Ash	5.5
Acid Insoluble Ash	2
Water soluble ash	2.5

Phytochemical Test of *Manilkara Zapota seed* extracts

Table: Phytochemical Test of *Manilkara Zapota seeds* extracts

Test	Petroleum Ether	Ethyl acetate	Methanol
1 Carbohydrate			
a) Molisch's test	+	+	+
b) Fehling's test	+	+	+
c) Benedict's test	+	+	+
d) Barfoed's test	-	-	-
2) Proteins			
a) Biuret test	+	+	+
b) Millen's test	+	+	+
c) CuSO ₄	+	+	+
3) Amino acids			
a) Ninhydrine test	+	+	+
b) Million's test	+	+	+
4) Alkaloids			
a) Dragendroff's test	-	-	-
b) Mayer's test	-	+	-
c) Hanger's test	+	+	+
d) Wagner's test	+	+	+
5) Glycosides			
a) Borntrager's test	-	+	+
b) Modified Borntrager's test	+	+	+
6) Flavonoids			
a) Shinoda test	-	+	+
b) Zinc hydrochloride test	+	+	+
c) Alkaline reagent test	+	+	+
7) Tannins			
a) Lead Acetate test	+	+	+
b) FeCl ₃ test	+	+	+
8) Steroids			
a) Sulphur powder test	+	+	+
b) Salkowski's test	+	+	+
c) Liberman- Burchard test	+	+	+
9) Test for Saponin (Foam Test)	-	-	-
10) Test for Gum	-	-	-
11) Test for Mucilage	-	-	-

+ Present, - Absent

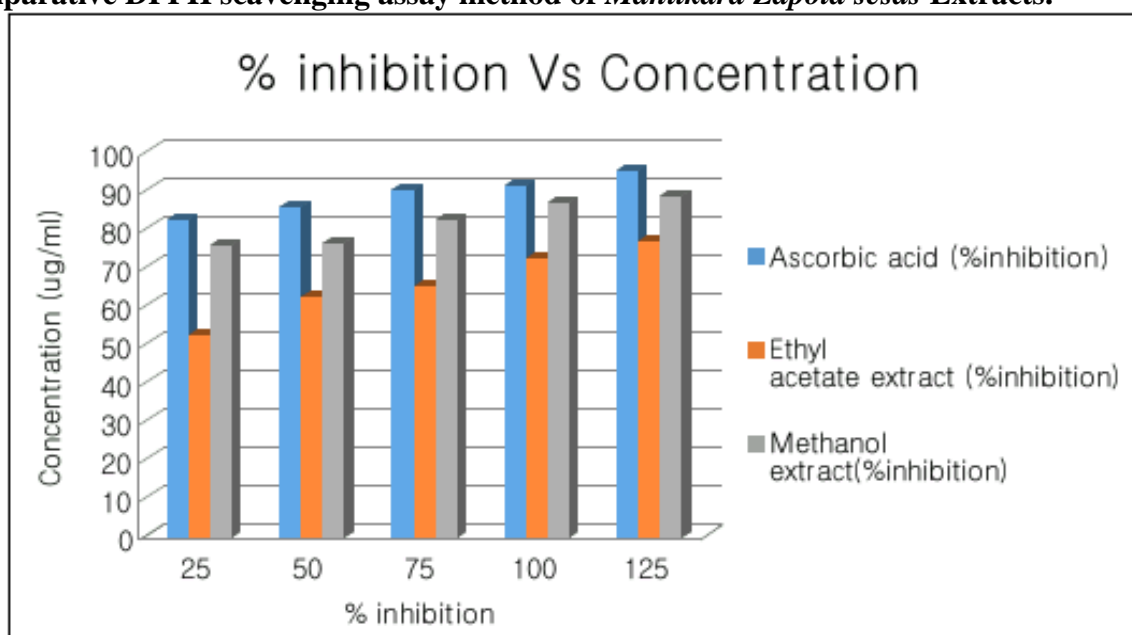
Preliminary Phytochemical evaluation of all extract were done, Petroleum ether, Ethyl acetate, Methanol shows presence of Carbohydrate, Protein, Amino Acids, Alkaloids, Glycosides, Flavonoids, Tannins, Steroids, Overall, Ethyl Acetate extract shows more results in Preliminary Phytochemical Evaluation.

Confirmation of phytoconstituents with Thin Layer Chromatograph.

Extract	SolventSystem	SprayingAgent	Rf value	Compound
Pet. Ether	Toulence: Ethyl Acetate(9:1)	Sulpuric Acid	0.07 0.10 0.32 0.75 0.81	Flavonone Protein Steroids Alkaloids Flavonoids
Ethyl Acetate	Toulene: Ethyl acetate(2:8:1)	Sulpuric Acid	0.24 0.83	Flavonoids Alkaloids
Methanol	Toulene Acetone: Formic Acid	Sulpuric Acid	0.12 0.36 0.65 0.86	Proteins Amino acid Alkaloids Flavonoids

Table: Thin Layer Chromatography**Antioxidant activity using DPPH(2,2-Diphenyl 1,1-Picrylhydrazyl) Scavenging activity**

Sr.no	Concentration	Ascorbic Acid (% inhibition)	Ethyl acetate extract (% inhibition)	Methanol Extract (% inhibition)
1	25	82.03	53.03	75.06
2	50	85.40	65.04	76.12
3	75	89.60	65.09	82.04
4	100	90.54	72.04	86.25
5	125	94.60	76.53	88.08

Table: DPPH(2,2-Diphenyl 1,1-Picrylhydrazyl)Scavenging activity**Comparative DPPH scavenging assay method of *Manilkara Zapota seeds* Extracts.****Graphic representation of % inhibition Activity at different Concentration of Ethyl acetate, & Methanol. Extract of *Manilkara Zapota seeds* with Standard.**

Effect of *Manilkara Zapota seeds* Extract in ethanol induced gastric ulcer

Group	Ulcer index	Ulcer protective%
Positive Control	32.42±0.66	0
Standard	7.1±0.53	92.90**
MZEA100	8.2±0.68	83.38**
MZEA200	8.1±0.36	86.98**
MZME100	32.53±0.98	64.98**
MZME200	27.98±0.89	69.66**

Table: Effect of *Manilkara Zapota seeds* Extract in ethanol induced gastric ulcer

Each value represent as mean ± SEM: n=6

** P Value is <0.001, hence there is high significant different between group.

(Analysis of Variance Test- ANOVA)

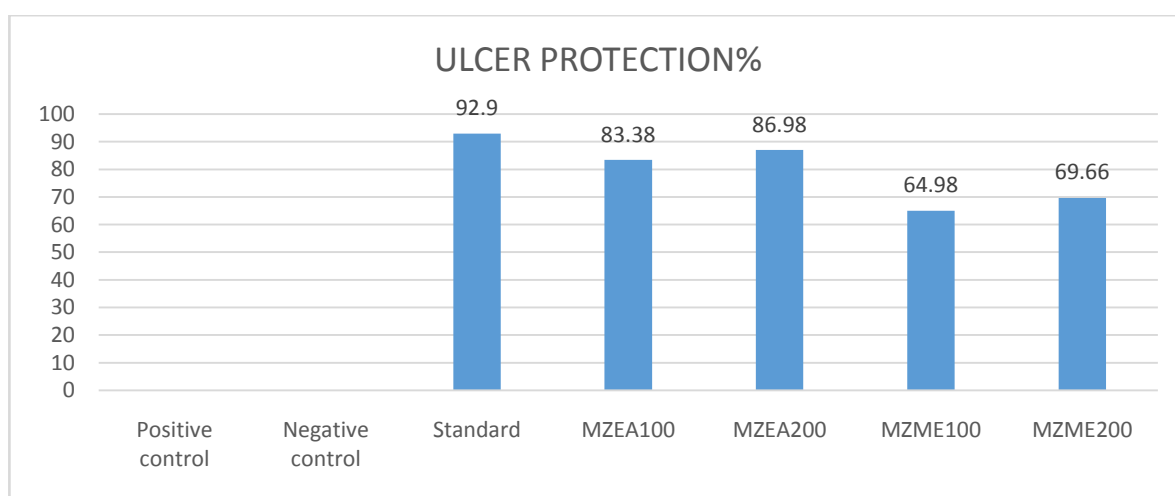


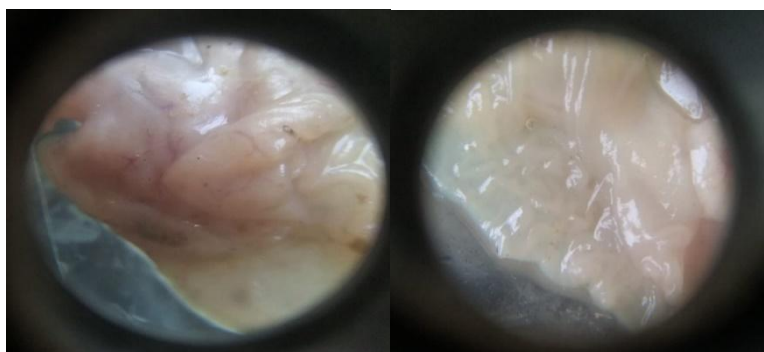
Chart: Ulcer protective %

Impact of MZEA and MZMA in pH and Total Acidity

Group	pH	Total acidity
Positive control	4.2±0.30	75.5±0.20
Standard	5.8±0.04	28.45±0.40
MZEA100	4.5±0.08	41.45±0.48**
MZEA200	5.3±0.11	28.55±0.13**
MZMA100	4.8±0.16	34.12±0.23**
MZMA200	5.0±0.25	44.78±0.46**

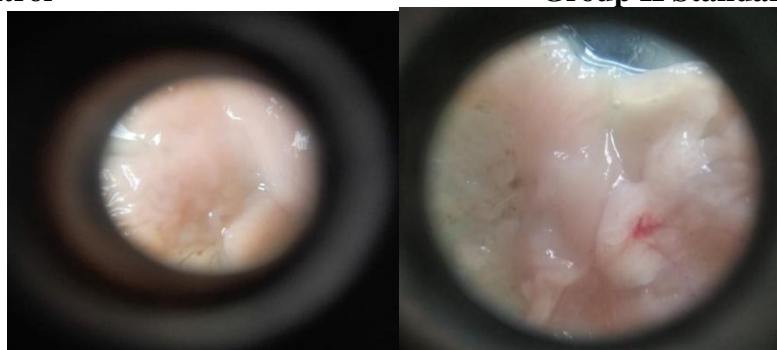
Table: Impact of MZEA and MZMA in pH and Total Acidity

Ethanol induced ulcer: Gross microscopic study of effect of *Manilkara Zapata seeds* extract on Gastric mucosal ulcer.



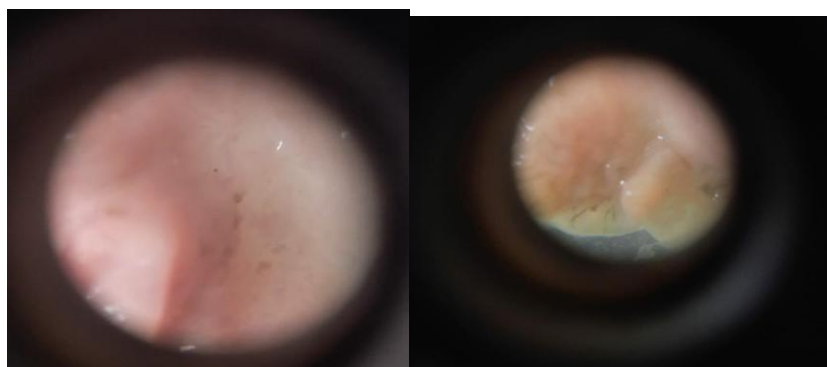
Group I: Control

Group II Standard (Ranitidine)



Group III. Ethyl acetate Extract (100mg)

Group IV Ethyl acetate(Extract 200mg)



Group V Methanol Extract (100mg) Group VI Methanol Extract (200mg)

From the above table it reveals that Ethyl acetate & Methanol extracts of *Manilkara zapota seeds* shows slight difference in gastric volume as compare to standard. The gastric juice were calculated which indicates acidity in stomach and which revealed that control Group D causing potentially increased acidity in stomach, while Standard and test extracts shows decrease in pH of gastric secretion.

Also, it reveals that Ethyl acetate and Methanolic extract of *Manilkara zapota seeds* has significant Anti-ulcer activity. Ethyl acetate shows 86.98% Inhibition. Methanolic extract shows 69.66% while Standard having 92.90% Inhibition from ulcer. Thus it reveals that Ethyl acetate extract at dose of 200 mg/kg has more potential than that of Methanolic extract.

Conclusion

The results of the current investigation unequivocally establish that the oral administration of Ethyl acetate (MZEA) and Methanolic (MZMTH) extracts derived from *Manilkara zapota seeds* exhibit considerable gastro protective efficacy in experimental animals with ethanol-induced gastric ulcers. This efficacy is substantiated by a notable reduction in ulcer index and a dose-dependent percentage

inhibition in both *In-vitro* and *In-vivo* models. These outcomes closely parallel the effects observed with the standard drug employed in the study. Beyond their antiulcer potential, the plant extracts also demonstrate promising activity against related ulcer-associated conditions, particularly oxidative stress.

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