

## **Crude Extract of Terminalia Chebula Fruit Effect on Gastro Intestinal Disorders Using Different Animal Models**

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### **ABSTRACT**

*Terminalia chebula* is an ancient medicinal herb. it is also known as Haritaki, Yellow myrobalan, Chebulic myrobalan, Yellow myrobalan, and *Terminalia chebulabe* longs to Combretaceae family is a major Ayurvedic medicine that is native to South Asia, predominantly from India. Apart from Ayurveda, it is commonly used in Unani and Homeopathic medicine systems. Because of the broad variety of pharmacological activities connected with the biologically active constituents found throughout this herb, it is included in conventional medicine. The fruit contains main pharmacological activities such as Hepatoprotective activity, Cytoprotective activity Cardioprotective activity, Antidiabetic and renoprotective activity, Antibacterial activity, Antifungal activity, Antiviral activity, Antiprotozoal activity, Anti-inflammatory and anti-arthritic activity, antioxidant and free radical scavenging activity, Anticarcinogenic activity, Antimutagenic, radioprotective and Chemopreventive activity, Hypolipidemic and hypocholesterolemic activity, Adaptogenic and anti anaphylactic activities, Gastrointestinal motility improving and anti-ulcerogenic activity, Antispasmodic activity, Wound healing activity, Anticaries activity, Immunomodulatory activity any many are reported with scientific evidence. All these ancient applications of *Terminalia chebula* as home remedies have been confirmed in preclinical trials. The current evidence on the effect of *Terminalia chebula* intake or consumption on gastrointestinal disorders and diseases is scientifically based on preclinical and clinical trials. All these ancient applications of *Terminalia chebula* as home remedies have been confirmed in preclinical trials. The current evidence on the effect of *Terminalia chebula* intake or consumption on gastrointestinal disorders and diseases is scientifically based on preclinical and clinical trials. Study indicates different dosage of *Terminalia chebula* is effective to get relief from gastrointestinal troubles. Due to less number of gastrointestinal studies, there is no scientific report to consume a specific amount of dose. To prove that *Terminalia chebula* and its standard extracts are effective as a gastroprotective agent, more comprehensive preclinical and clinical trials are required. To reliably evaluate the appropriate dosages for specific disorders and preparation of extract of *Terminalia chebula* fruit in prospective human trials procedures, dose-finding preclinical studies should be conducted. There is an evident need for more patient and physician education concerning specific therapies, legislation to regulate the quality of pharmaceutical preparations, and, in particular, more clinical and pre-clinical trials to determine the value and safety of such medicaments in digestive and other disorders.

**KEYWORDS:** Biologically active constituents, gastrointestinal disorders, Pharmacological activities, Preclinical studies, *Terminalia chebula*

### **ARTICLE DETAILS**

**Published On:**  
**23 December 2021**

**Available on:**  
<https://ijpbms.com/>

### **INTRODUCTION**

Increase the chances of completing a clinical course the trial that culminated in the approval of a new drug, the choice of

suitable preclinical models is identifying a healthy, powerful one, Efficient and effective drugs require thorough use of Preclinical research, which assesses aspects of

Pharmacodynamics, kinetics, and pharmacokinetics. Preclinical studies are the first step to move towards novel drugs, where researchers investigate the mechanism of action, Toxicity, safety, the efficacy of the drug. Progress in clinical science is highly dependent on addressing this question: How do various factors affect the human body, such as medications, chemicals, microorganisms, or hormones? Unfortunately, it is not easy to answer these issues by conducting relevant tests on human populations. Therefore, the creation of animal models that accurately imitate human PathoPhysiology research to create various circumstances of human disease is an acceptable alternative. A suitable preclinical study to demonstrate its safety and effectiveness and applicability is the most critical stage in the production of safe and reliable drugs. In recent years, drug recalls have become increasingly frequent, causing pharmaceutical companies to increase their commitment to the safety assessment of preclinical drugs. At present, in vitro and in vivo drug screening methods in preclinical applications are more advanced, but these technologies are expensive. With the rapid growth of computer science in recent years, In-Silico technology has been widely used to determine the related properties of drugs in the preclinical process and has developed numerous software programs and In-Silico models to further promote the in vitro research of ADMET. Preclinical research remains an essential tool for discovering and validating novel pharmaceutical products for gastrointestinal disorders. While in vitro assays can be used to check receptor-ligand interactions and to test the structural activity, only whole-animal studies can explain drug efficacy within the gastrointestinal system. Animals are models for the majority of gastrointestinal diseases. The objective of this chapter is to provide a critical assessment of common animal models used to develop drugs for gastrointestinal disorders. Models for upper gastrointestinal disorders involving the esophagus, stomach, and small intestines and lower gastrointestinal disorders that focus on the colon are presented for brevity. Ayurveda is a 5 000-year-old healing tradition rooted in ancient Indian culture is there. "This vast body of healing knowledge has recently come to the attention of Western medical researchers on the search for novel therapeutic compounds due to concerns about more invasive, costly, and potentially toxic mainstream practices sometimes referred to as "Mother of All Healing. One of the most revered medicinal plants i.e *Terminalia chebula* belongs to the Combretaceae family, which, due to the presence of a large number of different forms of phytoconstituents, has numerous medicinal activities to exhibit therapeutic pharmacological activity. *Terminalia chebula* contains tannins, phytosterols, triterpenoids and anthracene glycosides. name of all the of tannin and phenols are in *Terminalia chebula* are listed in the review article. Anthraquinone glycosides are present in pericarp of *Terminalia chebula* and their structures are reported. Miscellaneous compounds such as palmitic, steric, oleic,

linoleic and other compounds are reported. *Terminalia chebula* is a major pharmaceutical medicinal plant and has been used since ancient times in the Unani System of Medicine, Ayurveda to fight various diseases and infections due to its potential medicinal use. This herb has been considered a valuable and inexpensive source of specific phytoconstituents that are commonly used in the production of drugs with higher safety profiles and lower side effects. *Terminalia chebula* is used as traditional medicine by Europeans, Iranians, Greek, Roman, Arabic, and Indians to treat cold, fever, psychological and physiological disorders. People now rely on modern phytotherapy for a few days. In traditional Iranian medicine, the safety, efficacy, and the prescribed dose of *Terminalia chebula* have been stated. *Terminalia chebula* has a large variety of phytopharmacological activities to treat cancer, paralysis, cardiovascular disorders, arthritis, ulcers, leprosy, epilepsy, gout, etc., due to the existence of biologically active constituents. Antioxidants, anti-diabetic, anti-bacterial, anti-viral, anti-fungal, anti-cancer, anti-ulcer, anti-mutagenic, were documented Activities for healing. The role of a certain micronutrient present in *Terminalia chebula* on ingestion and used as gastro-intestinal medicine to improve micronutrient level in a community. The details of *Terminalia chebula*'s safe function in Gastrointestinal mucosa also generate a new viewpoint across several clinical trials to improve either refute this medication. *Terminalia chebula*, an aqueous extract from a natural plant, has been checked for possible antioxidant activity through Analysis of HPLC, UV, cyclic voltammetry and kinetic spectrometer proved as an effective oxidative since it is capable of shielding cell components from damage caused by radiation, it can be regarded as a Potential Radioprotectology. The U.S. Food and Drug Administration classifies *Terminalia chebula* fruit as "Generally Recognized as Safe" and monographs reported that *Terminalia chebula* as a ancient herb and drug have no side effects, drug interactions. In review, we summarize animal model evaluating the effect of *Terminalia chebula* ingestion in gastrointestinal disorders.

### ANIMAL MODELS FOR UPPER GASTROINTESTINAL DISORDERS

#### 1. Effect of Gastroesophageal reflux disease, peptic ulcer and NASID associated ulcers:

*Terminalia chebula* fruit extracts acts as antacid to treat ulcers in ulcer-induced animals. *Terminalia chebula* functions as a prokinetic gastrointestinal agent monitor the GERD characteristics successfully and thus they are closely associated with signs of globus syndrome. Animals are pretreated with *Terminalia chebula* hydro-alcoholic extract demonstrated a substantial decrease in lesion index, overall infected area, and proportion of lesion relative to the control community of aspirin, ethanol, and cold restriction stress-induced ulcer experimental models in rats. The pylorus-linked model, displays antisecretory activity, contributing to

a decrease in the amount of gastric juice, free acidity, overall acidity, and significantly improved gastric pH. In pylorus ligation and ethanol-induced ulcer models in Wistar rats, the anti-ulcer function of *Terminalia chebula* fruit methanolic extract was investigated. The common variable calculated in both models was the ulcer index. The extract (250 mg/kg & 500 mg/kg) showed a substantial ( $P < 0.01$ ) decrease compared to the control group in gastric thickness, free acidity, and ulcer index. *Terminalia chebula* extract have both antiulcerogenic and ulcer healing properties, which could have been due to their gastroprotective activity. It studied the gastro-protective function of chebulinic acid derived from the fruit of *Terminalia chebula*. Chebulinic acid was tested against models of gastric ulcers caused by cold restriction, aspirin, alcohol, and pyloric ligation in rats. Potential chebulinic acid anti-ulcer action greatly inhibited the activity of H (+) K (+)-ATPase relative to omeprazole, supporting its anti-secretory activity. *Terminalia chebula* anti-ulcer action tended to be balanced with a beneficial effect on the gastrointestinal mucosa, with the enhancement of the Brunner gland's secretory status included in the defense against duodenal ulceration. The anti-ulcer operation of a methanol extract of *Terminalia chebula* fruit been examined in pylorus ulcer-induced ligation and ethanol models in Wistar rats. From both models, the general parameter was really the ulcer index. *Terminalia chebula* methanolic extract at some doses generated substantial inhibition of gastric lesions caused by Pylorus ligation caused ulcer & Ethanol caused the gastric ulcer. Particular dose extracts showed a significant decrease in gastric volume, free acidity, and ulcer index. The findings of the present study indicate that methanolic extract of *Terminalia chebula* fruit has been found to possess both antiulcer and ulcer curing properties, which may be attributed to its anti-secretory action. In inner lining of stomach and small intestine ulcers can be created such as gastric ulcer and duodenal ulcer. Plant source *Terminalia chebula* is used to treat different diseases. Stress induced ulcers are developed by cold restraint method in wistar rats. *Terminalia chebula* extract results are compared with standard drug Rantidine. Significant results are observed with *Terminalia chebula* such as reduced ulcer size, ulcer number, gastric volume, Total acidity, mucin content. *Terminalia chebula* is protective against gastric ulcers.

### 2. Ulcerative colitis:

In this study, *Terminalia chebula* acts as anti-inflammatory drug. Colitis induced by trinitrobenzene sulfonic acid in rats. The administration increased colonic cellular injury and Stool output and inflammation but reduced body weight, which was altered by treatment with *Terminalia chebula* ethanolic extract, showed substantial results Antibacterial activity and increased antioxidants but decreased free radical species and myeloperoxidase activity and radicals are affected in colitis. Accordingly, Dried fruit pulp extract of *Terminalia chebula* cured colitis by encouraging Antioxidant status, reactive

species, reducing intestinal bacterial load, and Myeloperoxidase, which is liable for damage to tissues and interrupted healing. Colitis was developed in rats by intracolonic administration of Acetic acid and sulfasalazine was administered orally to rats. Acetic acid therapy resulted in a substantial improvement in colonic injury ratings, adhesions, and weight and histology revealed deformed cryptate, lymphocytic invasion, and edema in the rat colon. Acetic acid caused an increased fecal production with blood and mucus and decreased body weight and showed increased levels of free radicals and decreased status of antioxidants in colonic mucosal homogenate, but The ethanolic extract of *Terminalia chebula* showed a decrease in the score of colonic injury, weight and adhesion and improvement in tissues with decreased lymphocytic infiltration, a decrease in the level of free radical and an increased in the role of antioxidants in the colonic mucosal homogenate. Therefore, ethanolic extract of *Terminalia chebula* had substantial healing effects in colitis triggered by Acetic acid, which could be attributed to improved antioxidant and free radical scavenging behavior.

### 3. Diarrhoea:

The antidiarrhoeal properties of the aqueous extract of *Terminalia chebula* and the active fraction were calculated by wet drop, intestinal transit in mice and enteropooling in Wistar rats. Castor oil-induced diarrhoea determined the antidiarrhoeal fraction, and HPLC-ESI-MS identified its key constituents. The extract at specified doses decreased diarrhoea, impaired intestinal transit, and also decreased enteropooling capacity, accordingly. diarrhoea has been induced using castor oil in mice and the physical changes are observed in small intestine and liver. Lesions of the mice infected with extract have been relieved. In addition, the fraction of ethyl acetate was the active fraction of the aqueous extract of *Chebulae Fructus*, which reduced diarrhea. Thus *terminalia* extract exhibited antidiarrhoeal properties and the fraction of ethyl acetate was its most active fraction.

### 4. Gastric emptying disorder:

*Terminalia chebula* is a public choice to believe agent in Ayurveda for enhancing gastrointestinal motility. The Charles Foster rats were split into four groups: the first group treats with normal saline, metoclopramide administered to the second group of rats; atropine administered to third group rats. The fourth group of rats is treated with *Terminalia chebula* orally. All the drugs are injected intramuscularly, 30mins before start the experimental procedure. prokinetic and anti kinetic activities are established due to metoclopramide and atropine. Later, methylcellulose is mixed with phenol red. After 20mins starts observed gastric emptying. Metoclopramide substantially enhanced gastric emptying and motility was tried to block by atropine. The percent gastric emptying of *Terminalia chebula* was found to increase and can serve as a helpful alternative to prokinetic drugs.

### 5. Constipation:

For laxative operation, crude aqueous extracts of *Andrographis paniculata* and *Terminalia chebula* have been studied. Experiments found that, under constipation conditions, both extracts had the potential to improve laxative activity. In vivo, all herbal extracts are tested, and then the results of fecal production in rats are compared with reference drug bisacodyl. The extracts develop significant laxative activity due to the presence of phytochemical constituents in a dose-dependent manner.

### CONCLUSION

*Terminalia chebula* may be considered a healthy and potentially beneficial alternative choice for patients suffering from the effects of gastrointestinal disorders, based on the scientific data obtained from this systematic analysis. It seems that taking a specific dose of *Terminalia chebula* will assist with gastrointestinal problems. During breastfeeding, *Terminalia* did not cause any side effects or adverse events. *Terminalia chebula* and its phytoconstituents have been shown to target several immune cells, laying the groundwork for its use in the treatment of multi-factorial human gastrointestinal disorders including ulcers, constipation. Furthermore, much of the known activities of *Terminalia chebula* components are focused solely on in vitro and in vivo research, with the exception of a few clinical studies in certain gastrointestinal disorders, especially hemorrhoidal, irritable bowel syndrome in preclinical and clinical studies, and some other complications that may not be adequately powered to produce significant results. As a safe and cost-effective option, more comprehensive and well-controlled human trials are required to demonstrate its effectiveness as a gastroprotective agent. To reliably assess the appropriate dosage and formulation of *Terminalia chebula*, dose-finding trials should be performed.

### ACKNOWLEDGEMENT

This study is related to my project from the Research scholar of Delhi Pharmaceutical sciences and research University, India. I also appreciate my Guide to encourage and support me to do this survey.

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