WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A Review on Pharmacological Screening Methods of Antiulcer Durg

Mr. Narsale Prathamesh Balshiram, Sonali Vinod Uppalwar, Swati Pawar

Ideal Institute of Pharmacy, Wada, Palghar.413501
Gmail Id: prathameshnarsale16@gmail.com

ABSTRACT

Gastric ulcer formation is influenced by various factors such as steroid and non-steroidal drugs, cigarettes, alcohol, trauma, sepsis, shock, Helicobacter pylori, and stress. Stress is a more aggressive factor and is often used to produce ulcer models. Depression, accompanied by psychotic and somatic symptoms, is present in most patients with gastro intestinal system (GIS) ulcers. Antidepressants, such as fluoksetin, bupropion, dothiepin, maprotiline, mian-serin, trimipramine, idazoksan, monoaminooxidase -B (MAO-B) inhibitors, imipramine, amiltriptiline, and mirtazapine, have been reported to have anti-ulcerative effects. An increased vulnerability to depression and anxiety in experimental animals is paralleled with ulcer development in humans. Classic antidepressants and anxiolytics can significantly reduce stress ulcer formation, possibly to a greater extent than traditional therapies. Fluvoxamine, a selective serotonin reuptake inhibitor (SSRI), inhibits the CYP 1A2 enzyme, producing reactive oxygen species.

Ulcer diseases and their physiopathologic conditions are similar, with increased reactive oxygen species (ROS) levels indicating stress and indomethacin-induced gastric damage.

INTRODUCTION

Peptic ulcers are lesions of the skin or mucous membrane characterized by superficial inflamed dead tissue, with gastric ulcers occurring in at least 10% of the world population. These ulcers are caused by a lack of balance between gastric aggressive factors and gastric protective factors. Aggressive factors include increased secretion of HCL and pepsin, inadequate dietary habits, free oxygen radicals, consumption of NSAIDs and alcohol, stress, and infection of helicobacter pylori. Gastric protective factors include adequate gastric blood flow, secretion of prostaglandins, mucous, nitric oxide, bicarbonates, and growth factors.

Drugs such as anticholinergic, histamine H2 receptor antagonists, antacids, and proton pump inhibitors are commonly used for treatment of peptic ulcers. However, prolonged use can lead to serious adverse effects like thrombocytopenia, nephrotoxicity, hepatotoxicity, and impotence. There is a need for more effective and safe treatments for ulcers due to the unpleasant side effects of existing anti-ulcer drugs.

Peptic ulcer diseases are heterogeneous disorders that manifest as a break in the lining of the gastrointestinal mucosa bathed by acid and pepsin. They can be classified as oesophageal, duodenal, or gastric. Factors such as bad dietary habits, excessive intake of non-steroidal anti-inflammatory agents, stress, hereditary predisposition, and Helicobacter pylori infection account for over 70% of cases.

In recent years, there has been growing interest in alternative therapies from plant sources due to their perceived lower side effects, ease of accessibility, and affordability. Plants with traditional ethno medicinal uses in peptic ulcer management need to be screened for potential antiulcer activity and as sources of antiulcer lead compounds.

There are several models that are used to evaluate antiulcer medicines. However, the choice of a suitable model has proven to be difficult as each model has significant advantages as well as disadvantages. The choice of a particular model is sometimes influenced by local resources, the objectives of the study, the hypothesis being tested, or research questions being answered by the researcher. The choice of model may also depend on the relevance to the type of peptic ulcer dis- ease under investigation. Generally, preclinical experiments should be carried out in vivo and supported, when possible, with in vitro studies to explore the mechanisms of action of drug candidates with antiulcer activity. Some challenges associated with the various models for peptic ulcers are that, apart from information on their pathophysiological and biochemical bases being scanty, they are also scattered in the literature and not easy to find.[7]

STRESS ULCER THROUGH IMMOBILIZATION STRESS

PURPOSE AND RATIONALE

Psychogenic factors, such as stress, play a major role in the pathogenesis of gastric ulcers in man. The first report of the use of restraint as stress factor was published by Selye (1936). Hanson and Brodie (1960) and Bonfils et al. (1966) described methods to study the effect of anti-ulcer drugs on immobilization stress in rats.[11]

PROCEDURE

The study involves using Wistar rats and controls weighing 150-170 g for a test drug and placebo. The rats are anesthetized with ether, fixed together, and wrapped in wire gaze. They are suspended in the dark at 20°C for 24 hours and sacrificed in CO2 anesthesia. The stomach is removed, and the number and severity of ulcers are registered using a stereo-microscope. The experiment aims to understand the effects of the drug on rats. scores:

CRITICAL ASSESSMENT OF THE METHOD

The experimental model, which mimics psychogenic factors in gastric ulcer pathogenesis, has proven effective in treating various drugs such as antacids, anticholinergics, H2-antagonists, proton-pump-inhibitors, and neuroleptics, but is only used for final drug evaluation.

INDOMETHACIN INDUCED ULCERS IN RATS

PURPOSE AND RATIONALE

Non-steroidal anti-inflammatory agents like indomethacin and acetyl-salicylic acid cause gastric lesions in humans and animals by inhibiting gastric cyclooxygenase, reducing the production of prostacyclin.

The study involves 8-10 Wistar rats weighing 150-200 g, administered test drugs orally in 0.1% Tween 80 solution before oral indomethacin. Six hours later, rats are sacrificed in CO2 anesthesia and their stomachs removed. Formol saline is injected into the stomachs, stored overnight, and examined the next day. The lengths of longest diameters of lesions are measured and summarised to give a total lesion score for each animal, with the mean count for each group calculated.

The mean score in control rats is about 25 (range 20–28). Inhibition of the lesion production is expressed as percentage value.

IMPORTANCE

Drugs with antiulcer activity are crucial in treating and managing various gastrointestinal conditions, particularly ulcers. Ulcers are open sores or lesions on the stomach, small intestine, or esophagus, caused by factors like bacterial infection, excessive use of NSAIDs, stress, or excessive stomach acid production. Antiulcer drugs help in healing existing ulcers by reducing stomach acidity or directly targeting bacterial infections. They alleviate pain by reducing irritation and inflammation of the ulcerated area. They also prevent complications such as bleeding, perforation, and obstruction by treating ulcers promptly. Chronic ulcers can significantly impact a person's quality of life due to pain, discomfort, and dietary restrictions. Antiulcer drugs not only heal existing ulcers but also help prevent their recurrence, especially in cases caused by NSAID use. Some antiulcer medications, like proton pump inhibitors (PPIs) and H2 blockers, are used to manage conditions like GERD, which causes acid reflux and heartburn. Overall, antiulcer drugs play a crucial role in treating ulcers, providing relief from symptoms, preventing complications, and improving the overall quality of life for individuals suffering from these gastrointestinal condition.

MODIFICATION OF THE METHOD

Djahanguiri (1969) studied the ulcerogenic action of indomethacin, finding that gastric lesions can be induced by aspirin, reserpine, or cysteamine hydrochloride. Kitajima et al. (1993) investigated the role of endothelin and platelet-activating factor in indomethacin-induced gastric mucosal injury in rats. After subcutaneous injection of 25 mg/kg indomethacin, rats were sacrificed and their stomachs were filled. Exogenous PGE2 or PGI2 can prevent gastric lesions, while reserpine and cysteamine hydrochloride can induce ulcers in rats.

The study by Wallace et al. (1989) investigated the ulcerogenic activity of endothelin in indomethacin-pretreated rats using an ex vivo gastric chamber. Scarpignato et al. (1995) evaluated NSAID-induced gastric mucosal damage in rats by continuously measuring and recording gastric potential difference.

ETHANOL INDUCED MUCOSAL DAMAGE IN RATS (CYTOPROTECTIVE ACTIVITY)

PURPOSE AND RATIONALE

Intragastric application of absolute ethanol is a reproducible method to produce gastric lesions in experimental animals, which can be partially inhibited by drugs like prostaglandins. The protective effect against various irritants is called cytoprotective activity. Witt et al. (1985) described a method to objectively quantify the extent of ethanol-induced gastric lesions using a transmission densitometer to measure the optical density of the photographic negative of the stomach mucosa. Male Wistar rats weighing 250-300 g were deprived of food 18 hours before the experiment, and then administered either the appropriate vehicle or a cytoprotective drug 30 minutes prior to administration of 1 ml absolute ethanol. Untreated animals were included as controls. One hour after administration, the animals were euthanized with CO2, and the stomachs were excised, cut along the greater curvature, and gently rinsed under tap water. The subjective scores of the treated tissues were recorded, and photographs were taken and processed. A light transmission densitometer was used to evaluate the negatives, with lower optical density values indicating damage and higher densities indicating little or no damage.

CRITICAL ASSESSMENT OF THE METHOD

Prostaglandins provide cytoprotection in rats without antisecretory activity, but ulcer healing occurs at antisecretory doses. Therefore, a compound's cytoprotective property in rats may not predict its ulcer healing potential in humans.

CONCLUSION

his paper reviews experimental ulcer models for testing potential antiulcer agents, including plant medicines with ethnomedicinal uses against ulcers. It discusses the pathophysiological mechanisms underlying the lesions produced, helping investigators make a sound scientific judgment when selecting a model for evaluating a test agent. The paper also discusses available methods for scoring ulcers and identifies pitfalls in various approaches. Antiulcer drugs have significantly improved the management and treatment of ulcers, offering relief and healing to individuals. Mechanisms like reducing acid production, enhancing mucosal protection, and targeting bacteria have demonstrated efficacy in alleviating ulcer symptoms and promoting healing. However, the long-term efficacy and potential side effects necessitate ongoing research and monitoring. The future of antiulcer drugs lies in continued innovation, striving for safer, more targeted therapies that enhance healing and prevent ulcer recurrence while emphasizing holistic approaches that combine medication with lifestyle modifications for optimal outcomes.

REFERENCE

1. Ding SZ., Lam SK.,et al.,Prostaglandin, tumor necrosis factor alpha and neutrophils: causative relationship in indomethacin-induced stomach injuries. Eur J Pharmacol ,1998, 257-163.
2. Guidobono F., Pagani F., et al.,Protection by amylin of gastric erosions induced by indomethacin or ethanol in rats. Br J Pharmacol, 1997, 581-586.
3. Bayir Y., Odabasoglu F., et al., The inhibition of gastric mucosal lesion, oxidative stress and neutrophil infiltration in rats by the lichen constituent diffractaic acid. Phytomedicine, 2006, 584-590.
4. Goyal RK., et al., Elements of Pharmacology, B.S. Shah Prakashan, New Delhi,India, 17th edition, 2008.
5. Chan FKL., Graham DY., et al.,Review article: prevention of non-steroidal anti-inflammatory drug gastrointestinal complications - review and recommendations based on risk management. Aliment Pharmacolo Ther. , 2004; 1051-1061.
6. R. K. Goyal., et al.,Elements of Pharmacology, B.S. Shah Prakashan,New Delhi, India, 17th edition, 2008.
7. Bhargava K., Gupta M., et al.,Mechanism of ulcerogenic activity of indomethacin and oxyphenbutazone," European Journal of Pharmacology, vol. 22, no. 2, pp, 1973, 191–195
8. Rao CV., Sairam K.,et al., Experimental evaluation of Bopoca monniera on rat gastric ulceration and secretion. Indian Journal of Physiology and Pharmacology, 2000, 435-441.
9. Bickel M., Herling AW., et al., Antisecretory effects of two new histamine H2-receptor antagonists. Arzneim Forsch/Drug Res ,1986,1358–1363
10. Herling AW., Bickel M., et al., A substituted thienol[3.4-d]imidazole versus substituted benzimidazoles as H+,K+-ATPase inhibitors. Pharmacology 36, 1988 , 289–297
11. Hanson H., Brodie D., et al., Use of the restrained rat technique for study of the antiulcer effect of drugs. J Appl Physiol 15,1960, 291–294
12. Bonfils S., Perrier J., et al., L'ulcère de contrainte durat blanc. Méthode de pathologie expérimentale et test pharmacologique. Rev Franc Etud Clin Biol 11, 1966, 343–356
13. Djahanguiri B., et al., The production of acute gastric ulceration by indomethacin in the rat. Scand J Gastroenterol 4 1969 , 265–267
14. Kitajima T., Yamaguchi T., et al., Role of endothelin and platelet activating factor in indomethacin-induced gastric mucosal injury in rats. Digestion 54 1993 ,156–159
15. Borella LE.,DiJoseph JF., et al., Cytoprotective and antiulcer activities of the antacid Magaldrate in the rat. Arzneim Forsch/Drug Res 39, 1989 ,786–789
16. Franzone JS., Cirillo R., et al., Cytoprotective activity of deboxamet: a possible interference with prostaglandin and prostacyclin metabolism in rat gastric mucosa. Int J Tiss Reac 10, 1988 ,149–158
17. Takagi K., Okabe S., et al., A New method for the production of chronic gastric ulcers in rats and the effect of several drugs on its healing. Japanese Journal of Pharmacology. 1970, 418-421.
18. Michael A., Charles A., et al., In Vivo Models Used for Evaluation of Potential Antigastroduodenal Ulcer Agents.Hindawi Publishing Corporation.Vol: 1 June 2013.