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SYNTHESIS OF NOVEL DERIVATIVES OF THE DRUGS FOR PEPTIC ULCER

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ABSTRACT
The most common gastrointestinal disease, peptic ulcer is affecting the majority of population in the world. The major causes are well understood and thus, the requirement of antiulcer drugs is gaining with the providing increase in the disease. The present review focuses the synthesis of various derivatives of antiulcer drugs that will be helpful in the upcoming challenging for peptic ulcer.

KEYWORDS: Antiulcer drugs, Peptic ulcer.

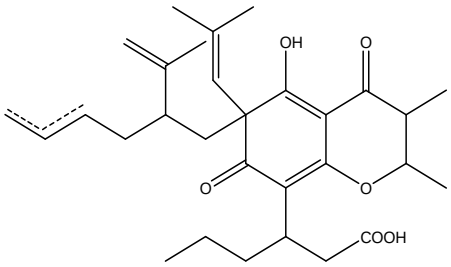
INTRODUCTION

Peptic ulcer is a gastrointestinal disease which affects the majority of population of the world. The gastric mucosal damage and the development of lesions is a complex occurring from an imbalance between gastroprotective (prostaglandin, bicarbonate, nitric oxide, blood supply, etc.) and aggressive factors (acid, pepsin) present in the gastric mucosa.[1]

In addition, in peptic ulcer, the *Helicobacter pylori* infection, frequent use of non-steroidal anti-inflammatory drugs and stress-induced mucosal damage are the major risk factors.[2] It is also well established that the reactive oxygen species play a crucial role in the pathogenesis of peptic ulcer, as the free radicals liberated from accumulated neutrophils and monocytes can cause oxidative damage to gastric mucosal cells by protein oxidation and lipid peroxidation.[3,4]

1. Evaluation of antiulcer activity of Chroma none fraction from Calophyllum brasiliensic Comb

The identification and isolation of various bioactive molecules from the hexane extract and latex of Calophyllum brasiliense's stem bark have been reported in the literature. These includes the isomeric chromanones brasiliensic and isobrasiliensic (1) acids, Inophylloidic acid (2), brasiliensophyllic acid A(3) the most active.[5]



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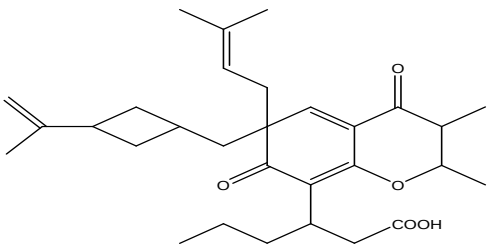

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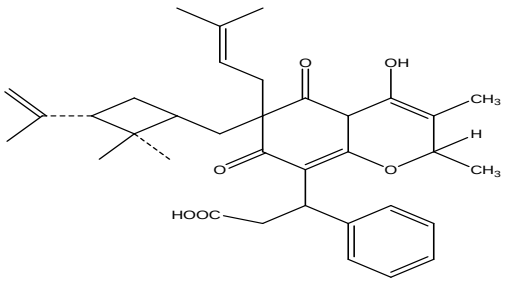

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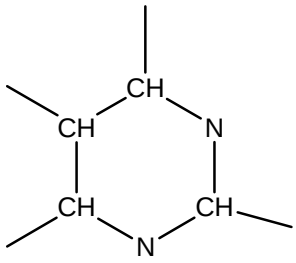
2. Synthesis and Anti-ulcer Activity of Some Dihydropyrimidines

Wide range of biological activities is associated with 1, 4-dihydropyridines/ pyrimidines, individually or in combination. In view of this, synthesis of various 6-methyl substitutedphenyl-2-thioxo-1, 2, 3, 4-tetrahydropyrimidine-5-carboxylic acid ethyl esters were undertaken for synthesizing biologically active molecules with improved activity. Anti-ulcer Activity, Dihydro pyrimidines (4), Thioethers (5), tetrahydropyrimidines (6)most active.[6]



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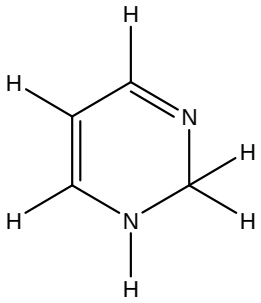

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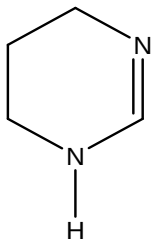

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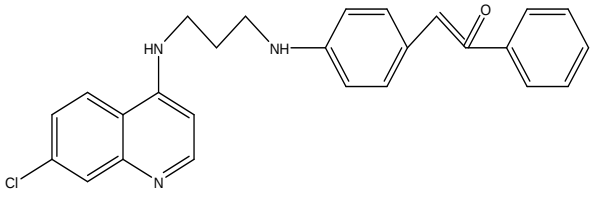
3. Identification of quinoline-chalcone hybrids as potential antiulcer agents

Antiulcer activity of novel quinoline-chalcone hybrids was investigated. Among them, eight compounds (7, 8, and 9) were found to be active in various ulcer models in Sprague Dawley (SD) rats. To understand the mechanism of action of these hybrids, the effects of the compounds on ant secretory and cytoprotective activities were studied. All these active hybrids improved the depleted levels of mucin. The additional experiments including the in vitro metabolic stability and in vivo pharmacokinetics led to the identification of compound 17 as an orally active and safe candidate that is worthy of further investigation to be developed as an antiulcer agent.[7]



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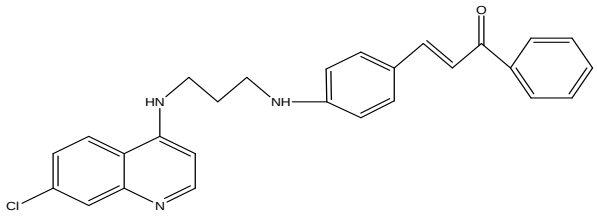

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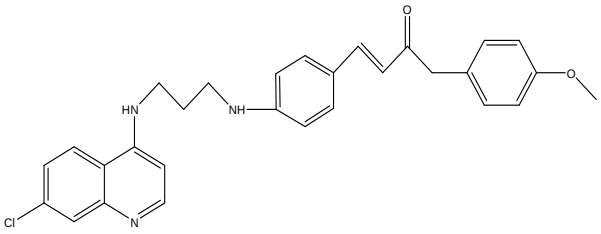

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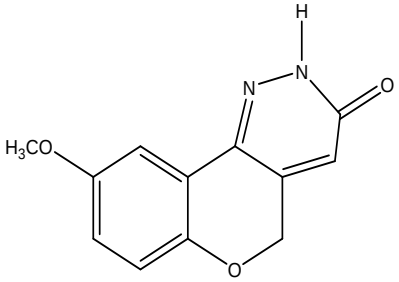
4. Tricyclic 3-(2H)-pyridazinone derivatives. Synthesis and evaluation of their antisecretory and antiulcer activity.

A new series of benzopyranopyridazinones either unsubstituted at the amide nitrogen or substituted by an alkyl thiourea, as well as two benzocinnolinone derivatives have been synthesized and tested for their antiulcer and antisecretory activity. All the test compounds showed statistically significant antiulcer properties in the EtOHmodel,[10] being the most active.[8]



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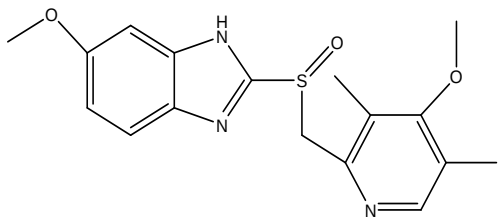
5. Simple, convergent synthesis of the pyrazole linked pyridine derivatives: Micro-wave, sonication and conventional methods

Organic molecules owe their biological activity to a variety of structural features. Sometimes a set of activities is associated with the structural backbone of a molecule. The antiulcer drug, Omeprazole (11), is a proton pump inhibitor (PPIs) and inhibits the action of hydrogen/potassium adenosine triphosphatase (Hþ/KþATPase) in parietal cells. Lansoprazole (12) is an antiulcer agent and proton pump inhibitor, Pantoprazole (13) suppresses the final step in gastric acid production by forming a covalent bond to two sites of the (Hþ,Kþ)-ATPase enzyme system at the secretary surface of the gastric parietal cell (11)(12)(13) being the most active.[9]



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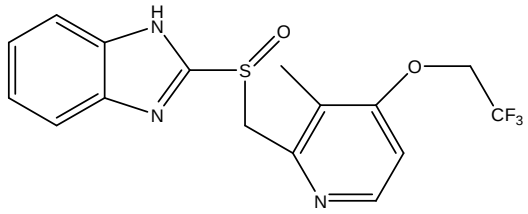

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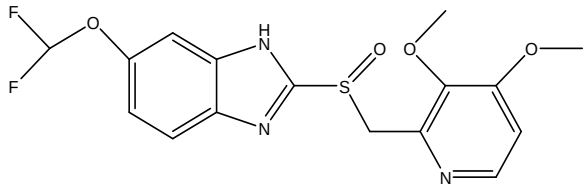

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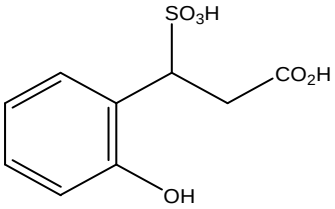
6. Synthesis and antiulcer activity of copperand zinc-containing coumarin antioxidants.

Coumarins represent a group of natural antioxidants of the phenol type and offer a broad spectrum of pharmacological activity. At the same time, they can be used as convenientreagents for passage to virtually any other type of antioxidants.[14] As is known, complex compounds of transition metals (in particular, copper) with simple organic ligandsmodel the reactions taking place at the active center of superoxide dismutase, a metalloenzyme containing copper and zinc cations.[15] We undertook the present study in order to synthesize new copper- and zinc-containing compounds and study their antiulcer activity.[10]



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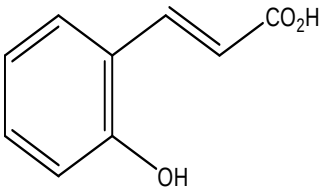

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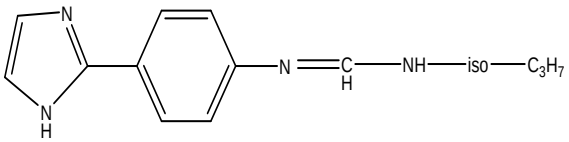
7. Studies on Antiulcer drugs. 4-furyl-2-guanidinothiazoles and Related compound as Potent histamine H2 – receptor antagonist

A series of 4-furyl-2-guanidinothiazole derivatives and related compounds were synthesized and evaluated for histamine H2- receptor antagonist and gastric acid antisecretory activities among them, compounds Mifentidine (16) Zaltidine (17) FCE-23067 (18) showed high activities in these tests some structure activity relationship are discussed.[11]



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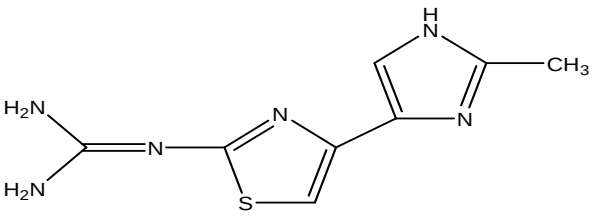

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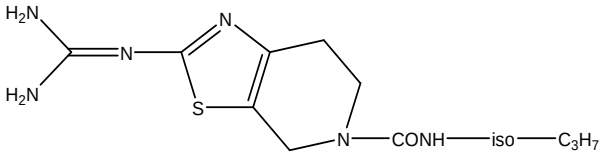

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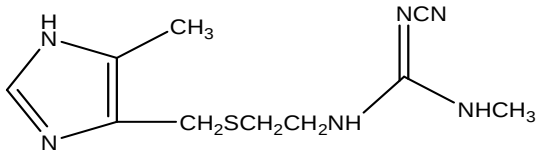
8. Studies on antiulcer drugs v1 synthesis and antiulcer of aralkylbenzazoles

A series of 2-alkylamino-5 or 6-aralky substituted Benzazoles were synthesized and tested for histamine h2- receptor antagonist and anti- stress activities these new compounds showed little or no histamine h2-receptor antagonist activity in contract to cimetidine (19) rantidine (20) famotidine (21) exerted higher activity than reference compounds the structure activity relationships of these compounds are discussed.[12]



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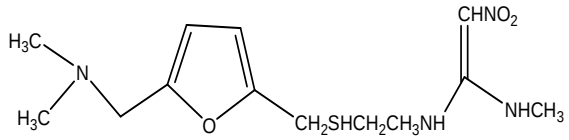

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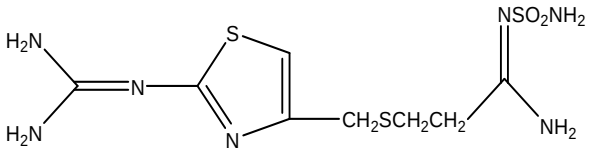

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CONCLUSION

The present review will help to understand peptic ulcer in detail. It covers the type and causes of peptic ulcer and also the various drugs that can be helpful to cure then peptic ulcer, the common gastrointestinal disease in preventing in the large no of population in the world. And thus the need to overcome this problem becomes more important.

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