



**INTERNATIONAL JOURNAL OF  
PHARMACEUTICAL SCIENCES**  
[ISSN: 0975-4725; CODEN(USA): IJPS00]  
Journal Homepage: <https://www.ijpsjournal.com>



## Review Paper

# Biochemical Mechanism of Healing Activity of the Natural Phenolic, Allylpyrocatechol Against Aspirin-Induced Gastric Ulceration

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## ARTICLE INFO

Published: 27 Jan. 2025

### Keywords:

erosion ,allylpyrocatechol  
,piper betel, stomach  
ulceration ,anti-  
inflammatory, antioxidant,  
cyclooxygenase.

### DOI:

10.5281/zenodo.14748904

## ABSTRACT

Peptic ulcers, characterized by mucosal erosion in the stomach or duodenum, continue to pose significant health challenges worldwide. Allylpyrocatechol, the active component obtained from ethanol extract of leaves of Piper betel. The study investigates the healing properties of a specific compound, allylpyrocatechol, which is derived from Piper betel. This compound is evaluated for its effectiveness against stomach ulceration induced by aspirin, a nonsteroidal anti-inflammatory drug (NSAID) known to cause gastric ulcers. allyl pyrocatechol (APC), the major antioxidant constituent of Piper betel, growth factors (EGF, EGF-R, SMAD-4) and cyclooxygenases (COX-1 and COX-2) were observed to be up-regulated in presence of APC during healing process.

## INTRODUCTION

Gastric ulcers are painful sores that develop on the lining of the stomach. They can be caused by various factors, including the use of non-steroidal anti-inflammatory drugs (NSAIDs) like indomethacin, which can lead to stomach damage and delayed healing. This is a significant health issue, including gastric ulcers [1]. as many people rely on NSAIDs for pain relief but may suffer from their side effects.(1) which are very commonly taken by the people as pain-killers. The NSAIDs induce ulcer by several mechanisms, one being the involvement of free radicals by neutrophil

activation. The free radical damage occurs mainly by the lipid peroxidation. There has been an accumulative evidence of the involvement of prostaglandin, cyclooxygenase 1 & 2, Nitric oxide, inducible Nitric oxide synthetase and different cytokines are induced or increased by gastric ulceration and might also contribute ulcer healing. There is a cross-over role of COX-1 and COX-2 (2) Piper betel leave extract contains large number of bioactive molecule like polyphenol, alkaloids, steroids, saponin and tannin. Piper betel has light yellow aromatic essential oil with sharp burning taste. The main constituents are Hydroxychavicol

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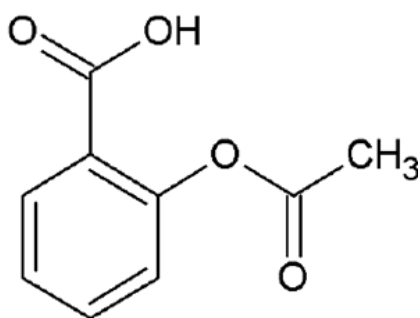
**Relevant conflicts of interest/financial disclosures:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



(HC)/Hydroxychavicol acetate (HCA), Allylpyrocatechol (APC) (3) Consequently, prevention of gastrointestinal disorder continues to be of concern for both medical professionals and researchers. Various synthetic anti-ulcer drugs are presently available, and some of these like misoprostol are specifically used to prevent or treat the NSAID induced gastric ulcer. However, each of these drugs confers simpler to severe side effects such as diarrhea, itching, skin rash, dizziness, and inactivation of some antifungal drugs (proton pump inhibitors), confusion in elderly patients, headache and antiandrogenic effect (H-2 receptor blockers), constipation, vomiting, indigestion, back pain, and dizziness (sucralfate), bleeding diathesis and abortion for pregnant women (misoprostol)[4] Thus, there is a growing interest on non-toxic, antiulcer formulations from medicinal plants, and many taxa of medicinal plants have been assessed worldwide for their antiulcerogenic effects. In the developing nations, this turn of events has also been prompted, in part, by the high cost of the modern antiulcer medication.

#### Peptic Ulcer :-

is a common gastrointestinal tract (GIT) disorder that affect about 10% of the world population . It's



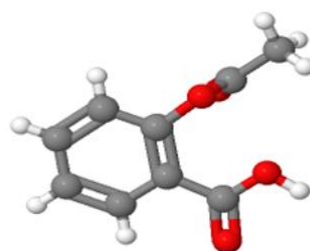
Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used for the treatment of pain and inflammation. Their use may result in gastroduodenal side effects[5] The current

characterized by GIT bleeding perforation and erosion of the mucosa wall due to imbalance between aggressive (acid, pepsin and *Helicobacter pylori*) and defensive factors (mucin, prostaglandin ,bicarbonate ,nitric oxide , mucosal blood flow and growth factors) . [8] Peptic ulcer is an acid-induced lesion of the digestive tract that is usually located in the stomach or proximal duodenum, and is characterized by denuded mucosa with the defect extending into the submucosa or muscularis propria [9] Annual prevalence estimates of peptic ulcer disease range between 0.12% and 1.5%. Peptic ulcer disease is usually attributable to *Helicobacter pylori* infection, intake of some medications (such as aspirin and non-steroidal anti-inflammatory medications), or being critically ill (stress-related), or it can be idiopathic.[10]

#### common signs and symptoms include:-

- Epigastric abdominal pain
- Bloating
- Abdominal fullness
- Nausea and vomiting
- Weight loss/weight gain

#### Aspirin Induced Peptic Ulcer :-



work was aimed to study the protective role of PRP on gastric ulcer induced by aspirin.

**Materials and Methods:** Forty adult male albino rats were divided into four groups. Group I; sham control, group II received PRP, group III received

aspirin for induction of gastric ulcer and group IV was provided with PRP then received aspirin. All rats were sacrificed then the fundic mucosa was processed for light and scanning electron microscopic study.(6)

**Mechanism :-** Reduced Mucosal Defense – Prostaglandins maintain mucus and bicarbonate secretion, which protect the stomach lining. With lower levels, the mucosal barrier weakens.

### **Piper Betel :-**

*Piper betle* L. (synonym: *Piper betel* Blanco) (Piperaceae) is a widely known perennial creeping plant belonging to the genus Piperaceae and originates from central and eastern Peninsular Malaysia and is distributed to East Africa and tropical countries of Asia.



### **Taxonomy**

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Piperales

Family: Piperaceae

Genus: *Piper* Species: *Piper betle* L.(8)

### **Distribution And Cultivation**

The betel vine is believed to have originated in Malaysia.(9) The plant is widely grown in forests that are generally damp and also in hot and moist climatic conditions of India and many other countries in South and South East Asia, viz. China and Vietnam. *Piper betle* is believed to have first emerged in tropical Asia and then spread to East Africa and Madagascar. Betel is widely grown in

India, Sri Lanka, Bangladesh, Indonesia, Nepal, Pakistan, Vietnam, Thailand, Laos, Kampuchea, Philippine Islands, Burma, Malaysia, Taiwan, Malay Peninsula and many countries in Southeast Asia and is known to have a long history, mentioning the presence of the betel plant over 2000 years.(10)

### **Microscopic Characteristics: -**

| Sr. No. | Parameters | Observation of Leaf            |
|---------|------------|--------------------------------|
| 1       | Color      | Yellowish Green<br>-Dark Green |
| 2       | Oduor      | Characteristic and pleasant    |
| 3       | Taste      | Sweet to Pungent               |
| 4       | Shape      | Heart shape                    |
| 5       | Texture    | Glossy, smooth                 |
| 6       | Venation   | Reticulate 8<br>Apex Pointed   |

### **Traditional Uses:-**

The oral cavity, which forms the initial part of the gastrointestinal tract, is an important organ involved in dietary intake, digestion. The oral cavity is affected by various ailments and globally dental caries, oral wounds, halitosis and cancer are some of the most common. Since time immemorial, humans have been using plants as dietary agents and the Indian indigenous plant *Piper betel*, commonly known as betel leaf, has been widely used in orodental care in the traditional Indian system of medicine Ayurveda.

### **Collection: -**

1. **Early Morning:** Betel leaves should ideally be collected early in the morning when they are fresh and have high moisture content. During this time, the leaves are more potent and richer in essential oils.
2. **Young Leaves:** The most medicinally potent leaves are usually young, tender ones that are not too mature. Older leaves might lose some of their medicinal properties.
3. **Post-Rain Season:** In many tropical areas, the period right after the monsoon season (when

the plants are healthy and lush) is considered a good time for harvesting, as the leaves tend to be fuller and contain more active compounds.

### Seasonal Considerations:

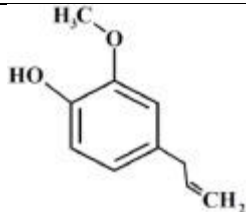
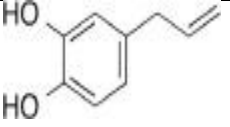
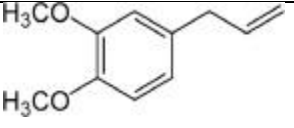
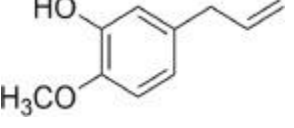
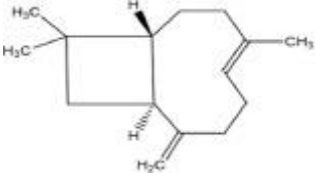
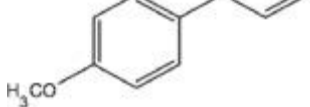
- **Rainy Season (Monsoon):** In many tropical regions, the rainy season is the peak growing period for betel leaves. The plants receive abundant water and nutrients, leading to better leaf quality. This season is typically preferred for collecting leaves, as they are more vibrant and packed with bioactive compounds.

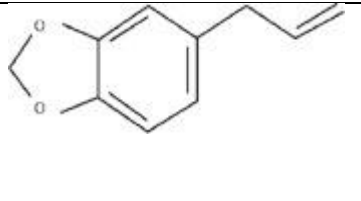
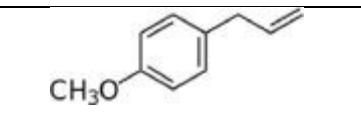
- **Dry Season:** During dry seasons, the leaves might become tougher and drier, reducing their medicinal potency. However, they can still be used, especially if no other fresh leaves are available.

### Harvesting Guidelines for Medicinal Use:

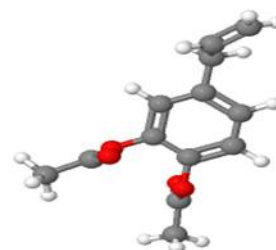
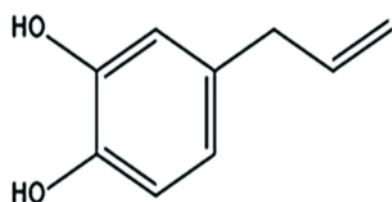
- **Fresh Leaves:** For most medicinal applications, fresh betel leaves are preferred, as they contain more moisture and active ingredients.

### Chemical Constituents: -

| Compound                | Chemical structure                                                                  | Biological properties                                                                                                                                       | Application                                                                                                                    |
|-------------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Eugenol                 |    | Anti-inflammatory, antimicrobial, antiviral, anti-mutagenic, analgesic, antioxidant, anti-carcinogenic, antiseptic, antidepressant, insecticidal, fungicide | Pain killer<br>oral hygiene                                                                                                    |
| Hydroxy chavicol        |   | Anti-inflammatory, antioxidant, antimutagenic, antibacterial, Anti-carcinogenic, antithrombotic, and gastric ulcer-healing activity.                        | Antimutagenic activity, use in mouthwash for preventing and treating oral infections.                                          |
| Methyl eugenol          |  | anti-inflammatory, cytotoxic against human cell lines, insecticidal activity                                                                                | Used as Fragrances and perfumery, toiletries, and detergents                                                                   |
| Chavibetol              |  | Noncentral analgesic, antipyretic, anti-inflammatory, antibacterial, antineoplastic                                                                         | Used as EO<br>The volatile and aromatic component                                                                              |
| $\beta$ - caryophyllene |  | Anti-inflammatory, anti-carcinogenic, pain relief, primary therapeutic against atherosclerosis and osteoporosis                                             | Used to prevent diabetes, endometriosis cerebral ischemia, anxiety and depression, liver fibrosis, and Alzheimer-like disease. |
| Chavicol                |  | Antimicrobial, antioxidant, antiseptic                                                                                                                      | used as an odorant in perfumery and as a Flavor                                                                                |

|           |                                                                                   |                                                                                                    |                                                                          |
|-----------|-----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Safrole   |  | Anti-inflammatory, detoxifying agent, antioxidant, antimicrobial, antimutagenic, immunosuppressive | beverage and candy preparation but carcinogenic to rats (not to humans). |
| Estragole |  | Antimutagenic, antifungal against some bacteria                                                    | Used as a flavoring agent, food additive, and EO                         |

### Allylpyrocatechol: -



ChemEssen.com

The general structure of a 4-alkylcatechol can be represented as 4-alkyl-1,2-benzenediol. The "alkyl" group can vary, leading to different specific names. For example:(11)

- 4-Methylcatechol: 4-Methyl-1,2-benzenediol
- 4-Ethylcatechol: 4-Ethyl-1,2-benzenediol
- 4-Propylcatechol: 4-Propyl-1,2-benzenediol

allylpyrocatechol, also known as 4-allyl-1,2-benzenediol, is a compound that belongs to the catechol family, which is characterized by the presence of a catechol moiety



- **Anti-inflammatory:**  
selectively Inhibits COX-2, reducing prostaglandin E2 PGI2(prostacyclin).
- **Gastroprotective:**  
Enhances mucin production, creating a protective gastric layer.
- **Antioxidant:**  
Neutralizes free radicals, reducing oxidative stress.
- **Hepatoprotective:**  
Prevents liver damage from reactive oxygen species (ROS).

| Property             | Ranges                                          |
|----------------------|-------------------------------------------------|
| Molecular Formula: - | <u>C<sub>9</sub>H<sub>10</sub>O<sub>2</sub></u> |
| Molecular Weight: -  | 150.17 g/mol                                    |
| Appearance           | White gray to crystalline powder                |
| purity (GC)          | mini. 98.0 %                                    |
| Melting point        | 43.0 to 49.0 °C                                 |
| Boiling Point        | 123 °C/2 mmHg                                   |
| Condition to Avoid   | Heat Sensitive                                  |

### APC's Effects:



| Interaction                               | Effect                              | Example                                                                 |
|-------------------------------------------|-------------------------------------|-------------------------------------------------------------------------|
| NSAIDs (e.g., Aspirin)                    | Synergistic anti-inflammatory       | Aspirin + Allylpyrocatechol: Enhanced anti-inflammatory effects         |
| Antioxidants (e.g., Vitamin C, Vitamin E) | Synergistic antioxidant effect      | Vitamin C + APC: Combined antioxidant effect in inflammatory conditions |
| Proton Pump Inhibitors (PPIs)             | Synergistic gastroprotective        | Omeprazole + APC: Enhanced protection against gastric ulcers            |
| Antiplatelet Drugs (e.g., Clopidogrel)    | Mildly enhanced antiplatelet effect | Aspirin + APC: Potential increased bleeding risk                        |

### Extraction of APC from Piper Betel

- **Source of APC:** Allylpyrocatechol (APC) is derived from the leaves of the Piper betel plant, which is commonly used in South East Asia as a mouth freshener. The leaves are known for their various health benefits, including antioxidant properties [12].
- **Extraction Method:** The technique used to extract APC is ethanol extraction. This involves using ethanol as a solvent to dissolve the active compounds present in the dried leaves. Ethanol is effective because it can extract a wide range of phytochemicals, including phenolic compounds like APC
- **Process of Extraction:**
- **Drying the Leaves:** The first step is to air-dry the Piper betel leaves. This helps to preserve the active compounds and makes them easier to extract. Air-drying is a gentle method that minimizes the loss of sensitive phytochemicals
- **Ethanol Extraction:** Once the leaves are dried, they are soaked in ethanol. The ethanol penetrates the plant material and dissolves the desired compounds, including APC. This process allows for the concentration of beneficial substances from the leaves

**Final Product:** The resulting ethanol extract contains APC along with other phytochemicals. This extract can then be used for further research

or therapeutic applications, particularly in studying its antioxidant and healing properties

### CONCLUSION: -

In this project we concluded that anti inflammatory action and gastroprotective action of APC from herbal origin are prepared and hence we can conclude that the piper betel leaves shows the anti inflammatory and gastroprotective properties that can use in inflammation and peptic ulcer APC syrup shows better activity less side effect compare to marketed aspirin. Frequently Aspirin intake causes the peptic ulcer due to APC syrup is safe in inflammation also in peptic ulcer. Oral administration of APC at different doses accelerated the rate of healing of gastric lesion induced by aspirin reduction in the production of NO, PGE2 and reduce expression of NF- $\kappa$ B. To conclude, the hydroalcoholic extract of *Piper betel* showed significant antiulcer activity in various experimental models of ulcer in rats suggesting its main mechanism of anti-ulcerogenic effect probably due to APC present in the extract. Herbal syrup of piper betel (APC) is safe for consumers and children and older patients in inflammatory condition or peptic ulcer show better therapeutic activity than the marketed formulation also hepatoprotective action no any side effect safe for use .

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**HOW TO CITE:** Kirti Pawar\*, Dipali Suryawanshi, Dhiraj Patil, Biochemical Mechanism of Healing Activity of the Natural Phenolic, Allylpyrocatechol Against Aspirin-Induced Gastric Ulceration, *Int. J. of Pharm. Sci.*, 2025, Vol 3, Issue 1, 2266-2274. <https://doi.org/10.5281/zenodo.14748904>