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Advances in Bioresearch

## ORIGINAL ARTICLE

# Anticataleptic effect of *Curcuma Amada* ethanolic extract in laboratory animals

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**ABSTRACT**
*Curcuma amada (Zingiberaceae) rhizomes in various extracts is reported to have mast cell stabilizing property and also the plant is reported to increase the release of dopamine from the brain. So, the current study was undertaken to scientifically validate the benefits of plant as an antihistaminic agent as well as dopaminergic agent. In the current research work, the antihistaminic activity of an ethanolic extract of Curcuma amada rhizome (at a dose of 200 mg/kg, i.p.) was evaluated using haloperidol-induced catalepsy and clonidine-induced catalepsy in laboratory rats. The results showed that the ethanolic extract exhibits the inhibitory effect on the catalepsy induced by the clonidine as well as haloperidol. This strongly suggests that, the inhibition is mediated through both antihistaminic and dopamine agonistic action. Hence, in the present study, it is concluded that, the ethanolic extract has significant anticataleptic activity. The polar constituents in the ethanolic extract of Curcuma amada may be responsible for the underlined effects.*
***Key words:** Antihistaminic, Curcuma amada, catalepsy bar, Haloperidol, Clonidine*

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## INTRODUCTION

Plants are one of the most important sources of biologically active substances. Secondary metabolites, which are physiologically active biochemical molecules, are responsible for a plant's medicinal properties. *Curcuma amada* is a medicinal herb belonging to *Zingiberaceae* family with various medicinal and biological properties. The purpose of this work is to evaluate the effect of acute administration of ethanolic extract of *C. amada* on the cataleptic behavior in the laboratory animals. Phytoconstituents abound in volatile oils isolated from *C. amada* rhizomes. The main phytocompounds present in the plant are curcuminoids (curcumin, dimethoxy curcumin, bisdemethoxycurcumin), phenolic compounds (caffeic acid, gentisic acid, ferulic acid, gallic acid, cinnamic acid), terpinoids (difurocumenol, amadannulen, amadaldehyde), and essential oils (myrcene and asarone). *C. Amada*'s medicinal properties are due to the presence of curcuminoids. It has anti-bacterial, anti-inflammatory, anti-tubercular, anti-cancer, anthelmintic, anti-allergy, and antipyretic properties and has been used for centuries to treat a variety of ailments. It also has the ability to heal a variety of skin diseases. [1]
The antibacterial activity was studied against different strains of microbes and higher efficacy of the same was observed with the essential oils prepared by Ultrasound-Assisted Extraction and Microwave-Assisted Extraction methods. [2] Difurocumenonol which was isolated from Mango ginger extract showed high antibacterial activity against gram-negative and gram-positive bacteria. [3] As per Ayurvedic, Unani and folk medicines, C. amada in its methanolic extract is used in the treatment of rheumatic disorder due to its analgesic property. It is also used in the treatment of inflammation and fever. [4] Due to its property as an appetizer, alexiteric, antipyretic, aphrodisiac, diuretic, emollient, expectorant and laxative and to cure biliousness, itching, skin diseases, bronchitis, asthma, hiccough and inflammation due to injuries; Ayurvedic and Unani medicinal systems have given much importance to it. The major chemical constituents found in Curcuma amada are starch, phenolic acids, volatile oils, curcuminoids and terpenoids like difurocumenonol, amadannulen and amadaldehyde. UV, IR, LC-MS and 2D-HMQCT NMR spectral data studies were used to deduce the structure of the isolated compound which was named as amadaldehyde, a novel compound. [5]

Mango ginger (*Curcuma amada*) is cultivated in India, Sri Lanka, Bangladesh and in many South-East Asian countries for its rhizomes. The rhizomes are used as flavoring agent in pickles and also dried rhizomes are used for flavoring curries and other dishes due to their medicinal properties. The ethanolic extract of its rhizomes showed presence of hydroxyl, carbonyl, ester and olefin functional groups and also methyl, methylene, methionine proteins and olefinic proteins. [6]

It is used as a carminative, digestive, stomachic, demulcent, febrifuge, and used in the treatment of anorexia, dyspepsia, flatulence, colic, bruises, wounds, chronic ulcers, pruritus, constipation, cough, sprains, gout, halitosis, otalgia. [6] The purified compound amaldehyde demonstrates antioxidant activity, cytotoxicity and platelet aggregation inhibitory activities. Biological activities of Mango ginger are hypotriglyceridemic activity, brine-shrimp lethal activity, enterokinase inhibitory activity, CNS depressant and analgesic activity. [5]

Catalepsy is a condition in which an animal holds an imposed posture for a long time before returning to its usual position. Catalepsy is a side effect of extrapyramidal drugs that disrupt dopaminergic transmission or increase histamine release in the brain. Clonidine, $\alpha_2$-adrenoceptor agonist, causes catalepsy in rats in a dose-dependent manner that is inhibited by H1-receptor antagonists but not by H2-receptor antagonists. We wanted to explore if there was any evidence for the plant's traditional use in asthma in this study, so we looked at its antihistaminic action.

## MATERIAL AND METHODS

### Plant Material:

The plant specimen of *Curcuma Amada* was collected from Pune District (Maharashtra) in January 2022, and was authenticated by the Botanical Survey of India, Pune. The plant accession number was AAGCL1.

### Animals:

Male Wister albino rats weighing 180-200 g were divided into three groups, each group containing six animals (for each model) and housed under standard laboratory conditions. The animals were provided free access to food and water. The protocol was approved by IAEC (Institutional Animal Ethical Committee) of Progressive Education Society's Modern College of Pharmacy, Yamunanagar, Nigdi, Pune-44.

### Drugs and chemicals

The drugs used were: Clonidine (Unimedicolab, Utttarakhand, India), Haloperidol (RPG Life sciences Ltd., Gujrat, India.), and Pheniramine Maleate (Sanofi India Ltd., Ankleshwar, Gujrat, India); all the drugs and chemicals were procured from available commercial sources. Chemicals used were: Ethanol analytical grade (New Neeta Chemicals, India) and Tween-80 analytical grade (New Neeta Chemicals, India).

### Preparation of Extract:

In this process, 1k g of finely ground rhizomes were kept in a well stoppered container macerated with 1L of analytical grade ethanol for the period of 3-days at room temperature with occasional agitation until the soluble portion is completely dissolved. The resulting mixture was then filtered and the subsequent marc was pressed and the extract was clarified with filtration after standing. The yield of the extract was found to be 20%.

### Phytochemical Analysis [7, 8]

Phytochemical analysis was done as per the reported procedure.

### Quantitative estimation of total phenolic and flavonoid content [9]

The extracts were quantified as per the reported procedure

### Anticataleptic activity

### Effect on clonidine-induced catalepsy:

The impact of extract on clonidine-induced catalepsy was investigated using the catalepsy bar test apparatus. Group-I was administered with saline into the rats (n=6), group-II was treated with ethanol extract (200 mg/kg, i.p.) and group-III was treated with the standard medication pheniramine maleate (10 mg/kg, i.p.). The inducer clonidine (1 mg/kg, s.c.) was administered 30-minutes before treatments. The extract dose was chosen based on the results of a previous acute toxicity study. [10] The catalepsy duration was measured at 0, 15, 30, 60, 90, 120, 150, and 180 minutes after the rat's forepaws were placed on a horizontal bar (1 cm in diameter, 12 cm above the table) and the time it took the rat to withdraw its paws from the bar was recorded for each rat.

### Effect on haloperidol-induced catalepsy:

The impact of extract on haloperidol-induced catalepsy was investigated using the catalepsy bar test apparatus. Group-I was administered with saline into the rats (n=6), group-II was treated with ethanol extract (200 mg/kg, i.p.) and group-III was treated with the standard Levodopa (30 mg/kg, i.p.). The inducer Haloperidol (1 mg/kg, i.p.) was administered 30-minutes before treatments. [10] The catalepsy duration was measured at 0, 15, 30, 60, 90, 120, 150, and 180 minutes after the rat's forepaws were placed on a horizontal

 

bar (1 cm in diameter, 12 cm above the table) and the time it took the rat to withdraw its paws from the bar was recorded for each rat.

**Statistical Analysis:**

The information is presented in the form of a Mean ± Standard error of the mean (SEM). The data was analyzed using a two-way ANOVA. Prism Graph Pad 8.4.3 was used for statistical analysis. *P<0.001 was used as the significance level.

## RESULTS

### A) Phytochemical Analysis

To evaluate the presence or absence of various phytochemical constituents, qualitative phytochemical testing of extracts was carried out using conventional methodologies. Carbohydrates, flavonoids, phenolics, lipids and oils, saponins, and other substances were discovered in phytochemical analyses of numerous extracts.

Table 1: **Phytochemical Constituents**

| **Phytochemical Constituents** | **Yes (+) / No (-)** |
|---|---|
| Carbohydrates | + |
| Flavonoids | + |
| Alkaloids | + |
| Triterpenoids | + |
| Tannins | + |
| Fat and oil | + |
| Steroids | - |
| Saponins | + |
| Glycosides | + |

### B) Quantitative estimation of total phenolic and flavonoid content

| **Table 2: Total phenolic content of extracts of Curcuma Amada Rhizomes** | |
|---|---|
| Extract | Total phenolic content (mg GAE/g extract) |
| Ethanolic | 101.40 ± 1.21 |

The quantity/concentration of phenols is calculated using the equation y=0.014x+0.103, where y is the sample absorbance and $R^2$=0.9990. The results are presented as a mean ± standard deviation (n=3). SD stands for standard deviation. GAE: Gallic acid equivalents, C Amada: Curcuma Amada.

| **Table 3: Total flavonoid content of extracts of Curcuma Amada Rhizomes** | |
|---|---|
| Extract | Total Flavonoid content (mg RE/g extract) |
| Ethanolic | 21.8333 ± 1.30 |

y=0.008x+0.179, where y=absorbance of samples and $R^2$=0.9950, denotes the quantity/concentration of flavonoids obtained from the equation: y=0.008x ± 0.179. The results are presented as a mean standard deviation (n=3). SD stands for standard deviation. Curcuma Amada (Curcuma Amada).

### C. Anticataleptic activity:

### 1) Effect on clonidine induced catalepsy:

 

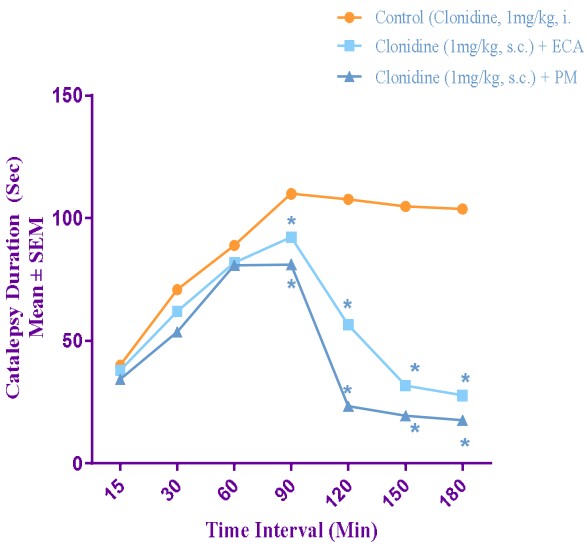


Fig 1: **Effect on clonidine induced catalepsy**

**The data was analyzed by Two-way ANOVA followed by Bonferroni's posttest. * (P<0.001) as compared to control group. ECA-Ethanolic extract of Curcuma Amada, PM- Pheniramine Maleate**

The results show that the duration of catalepsy induced by clonidine was significantly (p<0.001) reduced by the treatment with extract at 250 mg/kg, i.p. The effects offered by the extract were found parallel to the standard drug Pheniramine Maleate (10 mg/kg, i.p.).

**2. Effect on Haloperidol induced catalepsy:**

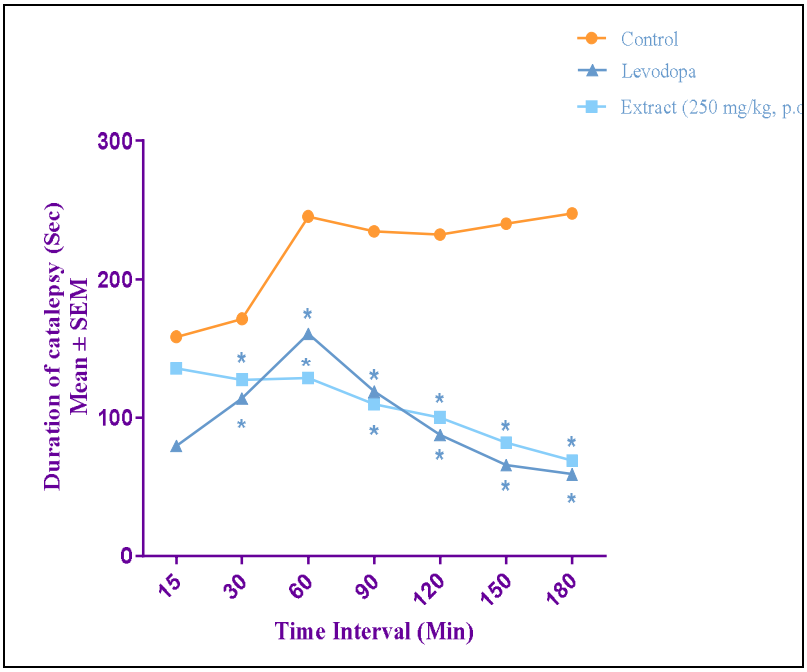


**Fig 2: Effect on Haloperidol induced catalepsy**

**The data was analyzed by Two-way ANOVA followed by Bonferroni's posttest. * (P<0.001) as compared to control group.**

Catalepsy duration was significantly reduced by the standard drug Levodopa. In parallel to this, there was significant effect on duration of catalepsy induced by haloperidol by treatment with extract (250 mg/kg, i.p.).

## DISCUSSION

Animals have been observed to develop catalepsy as a result of a variety of medicines [11]. Some researchers investigated the relative roles of acetylcholine and histamine in perphenazine-induced catalepsy and

 

proposed that antidepressants' anticholinergic activity could be attributable to an increase in dopamine levels in the brain or their capacity to suppress acetylcholine release. [12] The investigators also discovered that the amount of histamine in the brain appears to be directly related to the stage of catalepsy [13]. Uvnas investigated mast cell degranulation and its relationship to histamine release [14]. Clonidine releases histamine from mast cells [15]. It was also discovered that, pretreatment with L-histidine, a precursor of histamine, increased the potency of clonidine-induced catalepsy in a dose-dependent way [16]. It was reported that, in conscious mice, intracerebroventricular injection of histamine caused catalepsy, which was prevented by H1-receptor blocker but not by H2-receptor blocker.[17]

Prazosin, α-2-adrenoceptor blocker, inhibits clonidine-induced histamine release from mast cells. [18] Neuroleptics cause catalepsy as well, but by a different mechanism: they block dopamine D2-receptors in the substantia nigra. [19] This study found that an ethanolic extract of *Curcuma Amada* can prevent clonidine-induced catalepsy as well as haloperidol-induced catalepsy. The cataleptic action of clonidine in mice is mediated by histamine release from mast cells, according to this study. As a result, the polar components could be employed as an antihistaminic and in asthma treatment.

The active component curcumin was found to increase the brain dopamine levels. This extract's ability to prevent clonidine-induced catalepsy is most likely owing to its mast cell-stabilizing properties. Dopaminergic transmission is also found to be increased by the treatment of plant extract. Both MAO-A and MAO-B enzymes are inhibited by curcumin. It's worth noting that monoamine oxidase is the enzyme responsible for the breakdown of norepinephrine, serotonin, and dopamine. Curcumin enhances the concentration of these neurotransmitters at the synapse by reducing the activity of the MAO enzyme, therefore extending their action. [20]

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