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Original Research Article

Evaluation of antidepressant effect of aqueous extract of *Psidium guajava* leaves on Wistar albino rats

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ABSTRACT

Background: Depression is one of the common mental disorder prevalent worldwide. Use of herbal medicines in the treatment of depression is becoming popular because of adverse effects of existing non herbal drugs. In this study *Psidium guajava* leaf aqueous extract is screened for antidepressant activity in Wistar albino rats.
Methods: Wistar albino rats of both sex were used. After performing acute toxicity study, dose of test drug was fixed to 100mg/kg and 200mg/kg. Test and standard drugs were administered for 10 days orally. Standard drug used was Imipramine. Antidepressant activity was assessed using forced swim test and tail suspension test.
Results: Statistical analysis was done by one way ANOVA followed by Tukey Kramer. Aqueous extract of *Psidium guajava* leaves showed significant antidepressant activity. Both *Psidium guajava* aqueous extract (PGAE)-100mg/kg and 200mg/kg showed antidepressant effect but compared to 100mg/kg dose of PGAE, 200mg/kg showed significant antidepressant activity.
Conclusions: From this study it can be concluded that aqueous extract of *Psidium guajava* leaves has antidepressant activity.

Keywords: Aqueous extract, Antidepressant, *Psidium guajava* leaf, Wistar Albino rats

INTRODUCTION

Psidium guajava is commonly known as guava, is a plant which is grown in tropical and subtropical regions. It is a small tree approximately 10-15m in height. Leaves are oval in shape measuring 5-10cm in length. The fruit of this plant is edible and also used in folk medicine. It is used in ethnomedicine as an antimalarial. Infusions of the leaves are used for treating fevers, for diarrhoea and as a tonic in psychiatry.[1,2] The hydro-alcoholic extract of *P. guajava* was shown to decrease motor activity in mice. The leaves of *P. guajava* contain an essential oil rich in cineol, tannins and triterpenes. In addition, three flavonoids have been isolated from the leaves. Methanolic extract of guava leaves has got anti-inflammatory and analgesic activity.[3,4] Leaf extract has also been used as remedy for diabetes mellitus. Plant products are used as home remedies for minor ailments.[5,6] If research is done in this aspect it can be used effectively in treating many conditions.

According to WHO more than 320 million people suffer from depression worldwide. This burden is more common among South East Asians mainly China and India. Depressive disorders are one of the major health issue faced worldwide.

Depressive disorders are characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness, and poor concentration. Depression can decrease the quality of life. In severe cases, depression can lead to suicide.[7] Currently used drugs for the treatment of depression have numerous

side effects. A newer drug to treat this condition might be helpful for those who are suffering from this condition. The main objective of the study is to screen aqueous extract of *Psidium guajava* leaves for antidepressant activity in Wistar albino rats.

METHODS

This study is preclinical animal study. The study was conducted in the Department of Pharmacology Yenepoya Medical college Mangalore. Institutional Animal Ethics Clearance (IAEC) was obtained before conducting the study (YU-IAEC bearing No.4/9.6.2016).

Plant procurement

Fresh leaves of guava (*Psidium guajava* Linn.) were procured from the guava plants grown in Dakshina Kannada District. It was authenticated by botanist.

Preparation of guava leaf aqueous extract

Guava leaves were washed and cleaned. It was shade dried. Later it was powdered using a blender. The dried powder was wrapped in a muslin cloth and extracted using 1000ml of distilled water in Soxhlet apparatus maintained at around 70ºC - 80ºC for period of 3 days.[8] The extract was concentrated in the Rota- vapor at 60ºC and subsequently in the water bath for evaporation of solvent for a period of 2 days.

Animals

Healthy Wistar albino rats weighing 180-200g of either sex were included in the study. Obese and pregnant animals were excluded from the study. The animals were housed in standard cages at room temperature 28±2°C under the natural day and night cycles (12hr dark and 12hr light) with free access to diet and water.

Method

Acute toxicity study of aqueous extract of *Psidium guajava* leaves was performed following OECD guidelines 425.[9] No signs of toxicity was found at the maximum dose of 2000mg/kg body weight. The test dose was fixed to 100mg/kg and 200mg/kg body weight. Standard drug used was Imipramine-10mg/kg dose per orally.[10,11]

Animals were divided into 4 groups consisting of six animals each. Group I is control animals which were administered with distilled water per orally. Group II is standard drug which is Imipramine 10mg/kg per orally. Group III is test drug that is *Psidium guajava* leaf aqueous extract (PGAE) 100 mg/kg per orally. Group IV is test drug (PGAE) 200mg/kg per orally. The drugs were administered for 10 days and then assessed for antidepressant activity.

Assessment of antidepressant activity[10,11]

Forced swim test

Cylindrical containers were used which was filled with water. Rats were allowed to swim in the container filled with water one at a time after 1 hour of administering the test drug.

It was observed for 5 minutes each and time of immobility was noted, during which the rodent does not try to escape, and they just float to keep their head above the water. The values were compared with control and standard group (Figure 1).

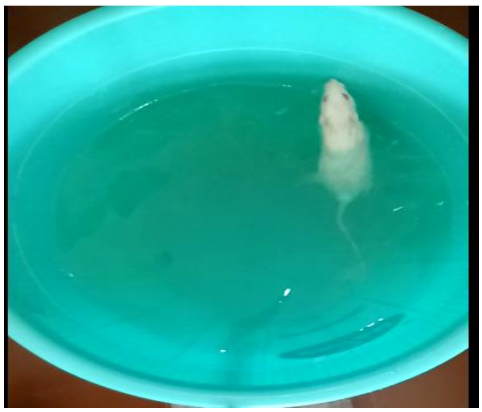

Figure 1: Forced swim test.

Tail suspension test

In this experiment rats were suspended from the edge of a table with help of adhesive tape placed approximately 1cm from the tip of the tail after 1 hour of administering the drug. They were observed for 5 minutes.

Duration of immobility was noted. Rats were considered immobile when they hang freely without any movements. Assessment was done based on duration of immobility. Decrease in the duration of immobility signifies antidepressant activity (Figure 2).

Figure 2: Tail suspension test.

RESULTS

Data was compiled and analyzed using the statistical package, GraphPad InStat software. Results are represented as Mean±SEM (standard error of mean). Statistical analysis was done by one way ANOVA followed by Tukey Kramer. p value <0.05 was considered statistically significant. P <0.01 were considered statistically very significant and p <0.001 were considered very highly significant.

Forced swim test

Time of immobility was observed in seconds in all the four groups. Control group (group I) of animals showed mean period of immobility of 84.16±3.76seconds, standard group (group II) showed mean period of immobility of 16.16±2.99seconds.

Table 1: Result of forced swim test.

Group	Immobile period (seconds)
Control-distilled water	84.16±3.764
Standard- Imipramine	16.16±2.994
Test drug-PGAE-100mg/kg	36.16±2.787*
Test drug-PGAE 200mg/kg	23.16±3.488**

*p value <0.001 compared to group I; **p value <0.001 compared to group I.

Group III and IV that is PGAE 100mg/kg and PGAE 200mg/kg showed mean period of immobility of 36.16±2.787 and 23.16±3.488 respectively. It was found that the period of immobility of both the test groups were less compared to control group of animals. p value was <0.001 when compared between group III and group I. Even p value was <0.001 when compared between group IV and group I. This shows that PGAE 100mg/kg and 200mg/kg possess very high significant antidepressant activity compared to control group. When compared between PGAE 100mg/kg and 200mg/kg, the later had more activity (Table1).

Tail suspension test

Table 2: Result of tail suspension test.

Group	Immobile period (seconds)
Control-distilled water	94.66±4.633
Standard- Imipramine	25.5±4.506
Test drug-PGAE-100mg/kg	58.16±4.30*
Test drug-PGAE 200mg/kg	36.16±3.97**

*p value <0.001 compared to group I; **p value <0.001 compared to group I.

The control group (group I) of animals showed mean period of immobility of 94.66±4.633seconds. Group II that is standard group administered with imipramine, showed mean period of immobility of 25.5±4.506seconds. Both the test groups, group III and IV showed dose dependent decrease in period of immobility that is 58.16±4.30 and 36.16±3.97 respectively. This test showed that period of immobility was less in both the test groups (group III and IV) compared to control group. p value was <0.001 compared to control group which signifies that it is statistically highly significant (Table 2).

DISCUSSION

Depression is a chronic psychiatric condition characterised by low mood and interest in life. There are many hypothesis which explains about depression. One among them is mono amino hypothesis which states that decreased levels of monoamines can lead to depression. One more hypothesis state that increase levels of serotonin can treat depression. Selective serotonin reuptake inhibitors act by increasing levels of serotonin. Currently used drugs in the treatment of depression acts mainly on monoaminergic system. They increase the monoamine levels and relieve depressive symptoms.[12]

Forced swim test and tail suspension test are the two common tests used to assess antidepressant activity of a drug in animal models. These models will create an environment where the animals cannot escape and will produce a condition in animals which is similar to depression in humans.

Forced swim test used to screen antidepressant drugs, is based on period of immobility of the rodents. Decrease period of immobility suggests that the test drug is having potent antidepressant activity. In present study, both doses of PGAE (100mg/kg and 200mg/kg body weight) showed dose dependent decrease in period of immobility which signifies that the extract has got antidepressant activity.

Tail suspension test is another test to assess antidepressant activity. It differentiates antidepressant from other drugs used for anxiety and psychosis.[10] PGAE 100mg/kg and 200mg/kg showed dose dependent decrease in period of immobility compared to control group. This suggests that PGAE has got significant antidepressant activity.

The antidepressant activity of *Psidium guajava* aqueous extract can be attributed to its phytochemical constituents. Literature shows that guava leaf contains flavonoids like quercetin and kaempferol.[2] Previous studies show that these flavonoids like quercetin and kaempferol has got significant antidepressant activity. There are studies demonstrating that quercetin and kaempferol inhibit mono amino oxidase enzyme.[13,14] So the possible mechanism of PGAE showing antidepressant effect can be due to the flavonoid components which inhibit monoamino oxidase enzyme. Inhibition of monoamino oxidase enzyme prevents oxidative deamination of biogenic amines (Adrenaline, noradrenaline, dopamine, and serotonin). Hence there is increase in levels of catecholamines and

serotonin leading to antidepressant effect.[12,14] Further studies and future research about neurotransmitter levels in this regard can confirm the exact mechanism.

CONCLUSION

The above study shows that *Psidium guajava* leaf aqueous extract 100mg/kg and 200mg/kg body weight, possess significant antidepressant activity in Wistar albino rats. PGAE 200mg/kg dose showed significant activity compared to 100mg/kg dose. Future studies in this aspect might reveal the exact mechanism which might be responsible for the antidepressant activity.

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