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# Anxiogenic effect on acute administration of gemifloxacin in rats

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## Abstract

**Objective:** Toevaluate the anxiogenic effect on acute administration of gemifloxacin in wistar albino rats. **Methods:** Elevated plus maze and open field test models were used. Rats were divided into four groups (n=6). All drugs used in the study were freshly prepared and administered orally, sixty minutes prior to the experiment. Group I (Control) received 10 mL distilled water, Group II received moxifloxacin (36 mg/kg), Groups III and IV received test drug, gemifloxacinat 50 and 100 mg/kg body weight respectively.The Results were analyzed using one way ANOVA followed by Dunnett's post hoc test. **Results:** There wasa statistically significant ($p<0.05$) decrease in total arm entries in elevated plus maze model compared to control. In open field test, the time spent in central squares was decreased whereas in peripheral squares was increased compared to control. **Conclusion:** The present studyshowedanxiogenic activity of gemifloxacin in wistar albino rats.

**Keywords:** Anxiogenic, Gemifloxacin, Moxifloxacin, Elevated plus maze model, Open field test.

## INTRODUCTION

Our Anxiety is a normal emotional behaviour. When it is severe and or chronic can precipitate or aggravate cardiovascular and psychiatric disorders.[1,2] Gemifloxacin, a broad-spectrum fluoroquinolone (FQ) hasgreater antimicrobial activity against gram-positive bacteria.[3,4] They are used in treatment of community acquired pneumonia and other respiratory tract infections caused by *Strep. pneumoniae, H. influenzae, M. catarrhalis*etc,.[5] Fluoroquinolones areknown to produce significant excitatory side effects on the central nervous system like headache, dizziness, insomnia, hallucinations, delirium, and seizures.[6] Earlier studies on rat with FQs (ciprofloxacin, norfloxacin and levofloxacin) showed anxiogenic effect in elevated plus maze model; moxifloxacin in elevated plus maze and open field test.[7-9] Hence the present study was undertaken to evaluate the anxiogenic effect on acute administration of gemifloxacin in wistar albino rats, using pharmacologically validated experimentmodels namely elevated plus maze (EPM) and open field test (OFT).

## MATERIALS AND METHODS

### Animals

Wistar albino rats of either sex weighing 150 - 200 g were used for the study.Three rats were housed in each polypropylenecages, in a controlled environment (22 ± 2°C) with a 12 hour light and dark cycle; they received standard rat chow (supplied by VRK Nutritional solutions, Sangli) and water *ad libitum.* . Animals were kept in experimental lab for seven days prior to experiment to acclimatize laboratory conditions. The study protocol was approved by the Institutional Animal Ethics Committee. Experiments were performed during the light phase of the cycle (9:00-15:00).

### Experimental design

*Drugs and dosage*

Moxifloxacin tablet (Cipla Pharmaceuticals Ltd.) and gemifloxacin tablet (Micro Labs) were obtained from the pharmacy of Srinivas Hospital, Mukka, Surathkal. All drugs were freshly prepared in distilled water just before the administration. Drugs and vehicles were administered orally in a constant volume

of 10 mL/kg. The doses were selected on the basis of earlier studies for moxifloxacin [9] and gemifloxacin [10]. In this acute study, drugs/vehicle were administered 60 min prior to experiment. Rats were divided into four equalgroups; six animals in each. Group I served as control (distilledwater, 10 mL/kg),Group II received moxifloxacin (36 mg/kg). Groups III and IV received gemifloxacin at 50 and 100 mg/kg body weight respectively.

**Behavioural assessment of anxiolytic activity**

*Elevated plus maze (EPM)*

The apparatus consisted of two open arms (length 50 cm X breadth 10 cm) and two closed arms of the same size emanating from a common central platform (10 x 10 cm). The two pairs of identical arms were opposite to each other. The apparatus was elevated to a height of 40 cm above floor level. Initially at the beginning of the experiment, rat was placed in the centre square of maze, with head facing one of the open arms. The time spent in open arms, entries in open and closed arms and numbers of rears in each arm in a five-minute exposure period were recorded. Thepresence of all four paws of rat in the arm was considered as an entry. The maze was carefully wiped, with hydrogen peroxide after each trial, to eliminate the possibility of bias due to the odour of the previous animal.[11,12]

*Open field test (OFT)*

The apparatus has a large rectangular wooden box (100 X 80 cm) with 60 cm high walls. The floor is made up of wire meshwith twenty-five squares (outer 16 and central 9). The experiment room was a sound attenuated, dark room. The box was illuminated with 40 W bulb, focusing on the field from a height of about 60 cm.After 60 min of drug treatment, ratswere placed individually ata peripheralcorner square in open field test; the number of peripheral and central squares crossed, time spent in central squares and number of rears were recorded for a five-minute period. The presence of all four paws in an arm was taken as an entry.[13,14]

**Statistical analysis**

Results were expressed as mean ± standard error of mean (SEM) and analysed by one-way ANOVA in software package SPSS (Version 17.0) with drug treatment as the independent factor. Post-hoc comparisons were performed by applying Dunnet's test. The results were considered statistically significant at $P < 0.05$.

**RESULTS**

**Elevated plus maze**

There was significant ($p<0.05$) reduction observed in the number oftotal arm entries,among rats treated with gemifloxacin (100 mg/kg) and moxifloxacin (36mg/kg); but gemifloxacin at both dosesdid not cause any significantdecrease in the number of open arm entries and rears in open arm compared to moxifloxacin (36mg/kg).The test drugs gemifloxacin and moxifloxacindid not produce any significant reduction in the time spent in open and closed arms as compared to control [Table - 1].

**Table 1:** Effect of gemifloxacin on behaviour of rats in elevated plus maze model

| Group (n=6) | Number of open arm entries | Number of total arm entries | Time spent in open arm (seconds) | Time spent in closed arm (seconds) | Number of rears in open arms |
|---|---|---|---|---|---|
| Control (10 mL/kg) | 8.00±0.44 | 12.33±0.88 | 75.17±15.30 | 224.83±15.30 | 13.50±0.76 |
| Moxifloxacin (36 mg/kg) | 4.00±1.00* | 5.83±0.47* | 37.00±10.58 | 263.00±10.58 | 6.50±0.61* |
| Gemifloxacin (50 mg/kg) | 7.33±0.33 | 11.83±0.87 | 69.83±13.76 | 230.17±13.76 | 11.83±1.19 |
| Gemifloxacin (100 mg/kg) | 6.50±0.67 | 9.00±0.81* | 56.67±12.82 | 243.33±12.82 | 10.67±2.23 |

(All values are expressed as mean ± SEM; *p < 0.05 as compared to control)

**Open field test**

The animals treated with gemifloxacin at 100mg/kg and moxifloxacin (36mg/kg) produced significant($p<0.05$) reduction in the time spent in central squares and increase in time spent in peripheral squares as compared to control. Gemifloxacin at both dosesdid not show significantdecrease in number of peripheral squares crossed ,increase in the number of central squares crossed and number of rears in peripheral squares as compared to moxifloxacin (36mg/kg) treated group. [Table - 2].

**Table 2:** Effect of gemifloxacin on behaviour of rats in open field test

| Group (n=6) | Number of Peripheral squares Crossed | Number of Central squares Crossed | Time spent in Peripheral squares (seconds) | Time spent in Central squares (seconds) | Number of rears in Peripheral squares |
|---|---|---|---|---|---|
| Control (10 mL/kg) | 22.33±1.56 | 15.83±1.37 | 253.00±1.52 | 47.00±1.52 | 16.67±1.66 |
| Moxifloxacin (36 mg/kg) | 33.17±2.63* | 10.67±1.62* | 280.67±1.99* | 19.33±1.99* | 9.17±0.94* |
| Gemifloxacin (50 mg/kg) | 24.17±1.74 | 14.83±0.94 | 258.17±4.96 | 41.83±4.96 | 14.67±0.80 |
| Gemifloxacin (100 mg/kg) | 27.33±2.04 | 12.67±1.35 | 267.83±3.63* | 32.17±3.63* | 13.17±1.07 |

(All values are expressed as mean ± SEM; *p < 0.05 as compared to control)

## DISCUSSION

Anxiety, like all emotions, has cognitive and neurobiological components. It is a negative emotion that occurs in response to perceived threats that can come from internal or external sources; can be real or imagined.[15]Elevated plus maze and open field test are commonly used test models used for behaviouralstudies in rats.[16,17]

The Elevated plus maze model helps toasses psychomotor performance and emotional state ofrodents. It involves spontaneous or natural aversive stimuli, i.e., height, unprotected area, and novelty.[18]Elevated plus maze test is based on a premise where exposure to open armsis more anxiogenic than closed arms.[19]Rats normally prefer to spend much of their allotted time in the closed arms; it reflects their aversion towards open arms whichaugment the fear towards open spaces. Drugs that cause decrease in open arm exploration are considered as anxiogenic.[20]Gemifloxacin (100mg/kg) and moxifloxacin (36mg/kg) treated groups showed decrease in the number of total arm entries compared to control, it is one of the important parameter indicateschange in general activity of rats.[21]

In open field test paradigm the unfamiliar situations, triggered by factors like individual testing and agoraphobia induces anxiety in rats.Anxious rats shows thigmotaxic behaviour by preferring periphery of the apparatus and reduced ambulation.[13] Anxiogenic agents inhibit exploratory behaviour of rats. The decreased time spent in central area and increased time spent in peripheral area atgemifloxacin (100mg/kg) and moxifloxacin (36mg/kg) treated groups wereobserved ; it indicates anxiogenic activity.[20]

In various experimental models of anxiety, expression of gamma-amino butyric acid ($GABA_a$) receptors and their subunits are modified by stress resulting in altered behaviour in rats.GABA ainhibitory neurotransmitter, known to play a vital role in anxiety.[22,23] The chemical structure of certain substituents of GABA and quinolones at their 7 position are similar.[24]The mechanism involved in CNS related adverse effects of fluoroquinolones is ill-defined.[25] Previous studies have revealed that ciprofloxacin,norfloxacin and moxifloxacin exert their anxiogenic effect may be by inhibiting the binding of GABA to its receptors.[7,8,9]The current study revealed anxiogenic effect of gemifloxacin (100 mg/kg) and moxifloxacin (36mg/kg) in both experimental test models compared to control.

## CONCLUSION

In conclusion, the observations demonstrate anxiogenic effect of gemifloxacin at higher dose(100 mg/kg) in Wistar rats. Nevertheless, further studies are necessary to elucidate the exact mechanism of action responsible for anxiogenic effect of gemifloxacin.

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**Conflict of Interest**: Nil

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