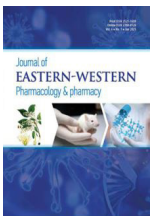

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ANTIARRHYTHMIC EFFECT OF GURGEM (*CARTHAMUS TINCTORIUS* L.) INJECTION ON AN EXPERIMENTAL ARRHYTHMIA MODEL IN MICE

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KEYWORDS

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ABSTRACT

Safflower (*Carthamus tinctorius* L.) is widely used in the treatment of cardiovascular diseases. Research has shown that safflower possesses significant biological activity, including inhibition of platelet aggregation, protection against myocardial ischemia, immune modulation, and antioxidant effects. Therefore, the objective of this study was to evaluate the effects of an injectable formulation derived from *Carthamus tinctorius* L. on cardiovascular function. Particular attention was given to the manifestation of these effects in clinical symptoms and the diagnostic value of electrocardiographic (ECG) analysis. For the experiment, an iWire-RX834-BIO4 ECG reader (iWorX Inc., USA) was used in conjunction with male BALB/c mice (n = 9), aged 6–8 weeks. The animals were divided into four groups: a healthy group (0.9% NaCl, n = 3), a negative control group (10% $CaCl_2$, 160 mg/kg, n = 3), a treatment group (Gurgem injection, 2.1 ml/kg, n = 3), and a positive control group (Verapamil injection). Differences between the groups were assessed based on changes in heart rate and specific ECG parameters (heart rate, R-R interval, and QT interval). ECG recordings were obtained for 20 minutes for all animals.

The average heart rate in the healthy group was 410 bpm. In contrast, the negative control group exhibited a 14.1% increase in heart rate, indicating tachycardia. However, in the treatment group receiving Gurgem injection, the average heart rate was 18.7% lower than that of the negative control group. Tachyarrhythmia is typically characterized by a shortened R-R interval, which can be detected via ECG. In the positive control group, the average R-R interval was 141.1 ms, whereas in the negative control group, it was reduced to 133.6 ms, reflecting a 5.2% decrease. In the treatment group, the R-R interval was extended by 20.8% compared to the negative control group, suggesting a positive modulatory effect on cardiac rhythm and tachycardia.

In conclusion, the injectable formulation derived from *Carthamus tinctorius* L. demonstrated therapeutic effects in an experimental model of arrhythmia (tachycardia), including stabilization of cardiac rhythm and reduction of heart rate.

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INTRODUCTION

In traditional medicine, the plant Safflower (*Carthamus tinctorius* L.) has been widely used to treat cardiovascular disorders. Researchers have found that this plant exhibits various pharmacological effects, including activity against heart disease, vascular inflammation, immune modulation, blood coagulation, thrombosis, antioxidant activity, hypoxia, and liver fibrosis[1–4]. Therefore, this study aimed to investigate its potential antiarrhythmic activity as part of the development of an injectable formulation derived from this plant and to examine its therapeutic effects in detail.

Disruption in electrical conduction can lead to arrhythmias and increase the risk of severe cardiac rhythm disorders in cardiovascular diseases. Arrhythmia is one of the common symptoms associated with cardiovascular conditions. Thus, evaluating the therapeutic effects of the Gurgem injection on cardiac arrhythmias is of significant importance.

MATERIALS AND METHODS

Animals: Male BALB/c mice (n = 12), aged 6–8 weeks, were used in the experiment. All mice were purchased from "Biocombinat" LLC. The animals were randomly assigned to four groups:

- **Healthy group**: injected with 0.9% NaCl as a vehicle (n = 3)
- **Negative control group**: injected with 10% $CaCl_2$ solution at a dose of 160 mg/kg (n = 3)
- **Gurgem treatment group**: injected with 10% $CaCl_2$ at a dose of 160 mg/kg, followed by Gurgem injection at a dose of 2.1 ml/kg (n = 3)
- **Positive control group**: injected with 10% $CaCl_2$ at a dose of 160 mg/kg, followed by Verapamil injection (standard treatment) (n = 3).

The animal experiment was conducted in accordance with the "Biomedical Ethical Guidelines for Animal Experimentation."

Reagents: The 10% $CaCl_2$ solution and Gurgem 2 ml injection were manufactured and provided by Tsombo Pharm LLC.

Experimental design: To induce a tachycardia model, 10 minutes after the intramuscular injection of Gurgem injection or Verapamil, a 10% CaCl2 solution was injected intravenously into experimental mice at a dose of 160 mg/kg. Following the induction of the pathological model, heart rate (HR) and several ECG parameters (RR interval, QRS, and QT interval) were monitored at 5, 10, 15, and 20 minutes to evaluate changes in cardiac tachyarrhythmia (Figure 1)[5, 6].

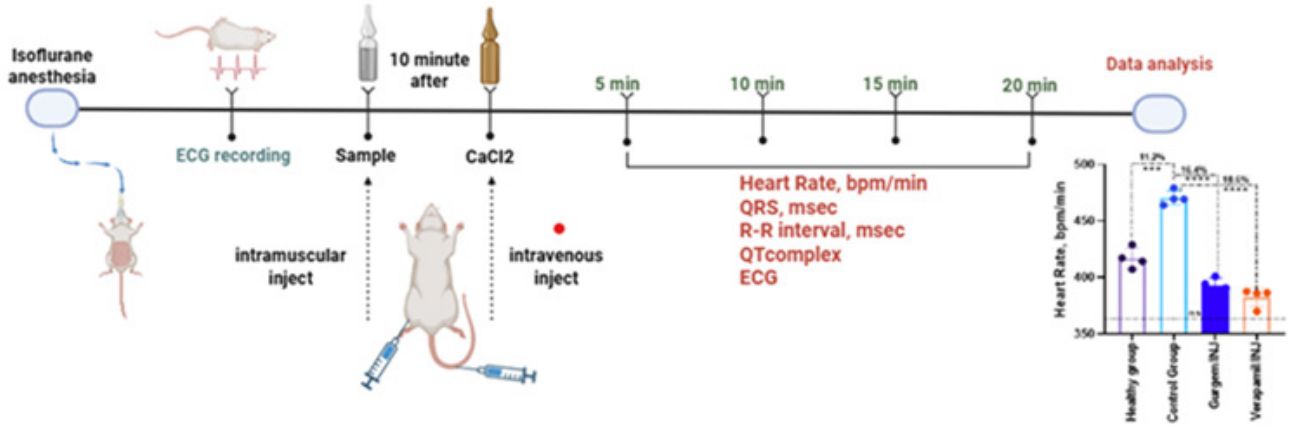

Figure 1. Experimental outline of calcium chloride-induced Tachycardia model

Results

This study evaluated the effect of Gurgem injection on calcium chloride-induced cardiac tachycardia, and the findings were analyzed as follows. In the ECG recordings (Figure 2A) of animals in the Healthy group, a regular rhythm was observed, with R waves of normal amplitude, visible P waves, and QRS complexes without abnormal ST segment widening or elevation. In contrast, the ECG of the Control group, in which arrhythmia was induced using $CaCl_2$, showed decreased R wave amplitude and prolonged ST segment duration, indicating an abnormal rhythm. The heart rhythm was irregular, with varying R-R intervals. At 10 minutes after calcium chloride injection, the R-R interval shortened, confirming the successful induction of a tachycardia model. In animals treated with the Gurgem injection, ECG recordings showed a gradual stabilization of heart rhythm beginning at the 15-minute mark, with increased R wave amplitude and more consistent waveforms. Similarly, in the Verapamil-treated group, the ECG showed a regular rhythm without signs of arrhythmia. These findings indicate that the Gurgem injection exhibits a stabilizing effect on cardiac conduction, comparable to that of Verapamil injection (Figure 2A).

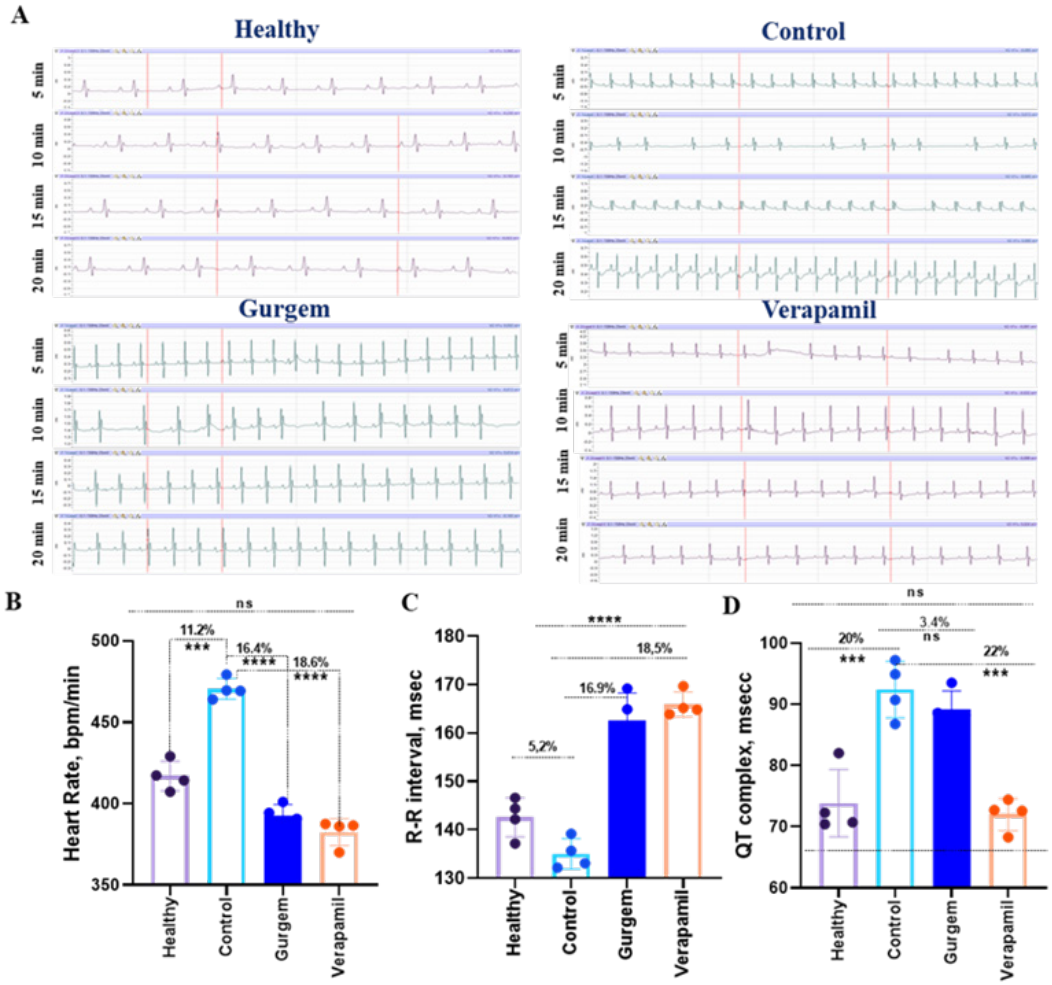

Figure 2. Effects of Gurgem injection on calcium chloride-induced tachycardia: A. ECG recordings of control and treatment groups; B. Analysis of Heart rate of experimental groups; C. Analysis of R-R interval of experimental groups; D. Analysis of QT Complex of experimental groups. The experimental data were statistically analyzed using one-way ANOVA in Graph Pad Prism 8. A p-value of less than 0.05 was considered statistically significant.

Heart rate (Figure 2B): The ECG of the Healthy group showed a heart rate ranging between 410 and 430 bpm. In the Control group, HR increased by 11.2%, confirming the presence of tachycardia. Compared to the Control group, HR decreased by 16.4% in the Gurgem-treated group and by 18.6% in the Verapamil-treated group. No statistically significant difference was observed between the two treatment groups.

The R-R interval (Figure 2C) in the ECG of the Control group was reduced by 5.2% compared to the healthy group, correlating with the increased heart rate. In the Gurgem-treated group, the R-R interval was prolonged by 16.9% compared to the Control group. For the Verapamil-treated group, R-R interval decreased by 18.5%, indicating that both treatments effectively reduced Heart Rate (HR) Analysis and restored normal rhythm. Regarding the QT interval (Figure 2D), ECG recordings after calcium chloride injection revealed broadened, elevated, and prolonged QT intervals. The QT interval in the control group was prolonged by 20% than that of the healthy group.

DISCUSSION

Heart rate (HR) is a fundamental physiological parameter that indicates how many times the heart contracts in one minute and is typically calculated based on the RR interval observed on an ECG. The normal HR for laboratory mice ranges between 500–700 beats per minute (bpm/min). In our study, HR Analysis of healthy mice ranged between 430–450 bpm. This slight deviation is likely associated with the type of anesthetic agents we used. In case of the ketamine-xylazine mixture, the mouse HR significantly dropped to 150–180 bpm, leading to severe bradycardia. In contrast, using isoflurane showed relatively minimal effects on heart rhythm. Therefore, the type of anesthesia used when studying cardiac rhythm significantly affects the result of the experiment, which is consistent with our findings and those reported by other researchers [7].

In milliseconds, the R-R interval is the duration between two successive R waves on the ECG and reflects the frequency of cardiac depolarization cycles. This interval includes the propagation of impulses from the sinoatrial (SA) node through the atrioventricular

(AV) node and the His–Purkinje fibers to the ventricles, up to the initiation of the next impulse. According to our results, the average RR interval in healthy mice was 140–150 milliseconds. When tachycardia is induced by calcium chloride, the RR interval is shortened to an average of 120 milliseconds. These findings align with other reports, where an HR of 414.1 bpm corresponded to an RR interval of 145 milliseconds, and an HR of 760 bpm was associated with an RR interval of 79 milliseconds [8]. These data support our observations that the RR interval shortens as HR increases and lengthens as HR decreases, which is visualized on the ECG as compressed or widened intervals between R waves.

The QT interval on the ECG represents the time from the beginning of the Q wave to the end of the T wave, encompassing both ventricular depolarization and repolarization. In our study, the QT interval increased by 20% in the control group compared to the healthy group. Following treatment with Gurgem injection or Verapamil injection, the QT interval decreased, which was consistent with the slowing of HR. This observation reflects the established relationship between cardiac electrical cycle frequency and the QT interval: when HR increases, the QT interval tends to lengthen, and when the HR decreases, it shortens. These results are in agreement with theoretical models describing this inverse correlation [9].

CONCLUSION

Gurgem injection demonstrates pharmacological efficacy in stabilizing cardiac arrhythmias on calcium chloride-induced ventricular tachycardia.

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Conflicts of Interest: “The authors declare no conflict of interest.”

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