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Research Article

CARDIOTONIC ACTIVITY OF AQUEOUS FLOWER EXTRACT OF *BOUGAINVILLEA GLABRA*

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ABSTRACT

The present study was undertaken to evaluate cardiotonic activity of aqueous flower extract of *Bougainvillea glabra*. Cardiotonic effect of aqueous flower extract of *Bougainvillea glabra* was studied by using isolated frog heart perfusion technique (Syme's Technique). Half Calcium Ringer solution was used as vehicle for administration of aqueous extract of *Bougainvillea glabra* as a test extract and digoxin as a standard. A significant increase in height of force of contraction (positive inotropic effect) and increase in heart rate (positive chronotropic effect) was observed with test extract as compared to the same dose of a standard digoxin and Adrenaline and the positive ionotropic effect of aqueous flower extract was blocked by beta receptor blocker. The present results indicated that a significant increase in height of force of contraction with increase in heart rate was observed as the dose of test extract increased.

Keywords: Syme's Technique, Digoxin, *Bougainvillea glabra*, Cardiotonic activity.

INTRODUCTION

Cardiac disease is an important cause of premature death in industrialized countries. It is estimated that cardiac disease will emerge as single largest contributor to morbidity in India accounting for nearly one third of total deaths in near future. Cardiac glycosides and catecholamines have been used as main therapeutic agent in the treatment of congestive cardiac failure[1]. However, the danger of cardiac glycosides intoxication is well documented[2] and doubts have been expressed about their effectiveness. Despite continuing advancement in understanding the basic pharmacology of cardio active drugs, cardiac glycosides, intoxication with digitalis a narrow therapeutic index drug remains a common clinical problem. Synthetic catecholamine has been reported to cause a severe oxidative stress in the myocardium through free radical formation[3]. It necessitates research for new drug and with this aim we have chosen *Bougainvillea glabra* and evaluated its cardio active potential.

Bougainvillea was named after the world traveler, Louis de Bougainville, who discovered it in Brazil in 18th century and brought it to Europe where it became both widespread and popular[4]. It is a member of the Nyctaginaceae family with close relatives being the four o'clock and the sand verbena[5,6]. Genus *Bougainvillea* includes eighteen species native of tropical and subtropical regions of south America from brazil west to peru south thouthern Argentina[7]. *Bougainvillea glabra* "Snow White" is a cultivar of *Bougainvillea glabra,* family: Nyctaginaceae[8]. All superficial feature of this cultivar is same as the *Bougainvillea glabra* but the bracts of this cultivar are white with greenish veins[9]. *Bougainvillea* commonly name as the paper flower owing to bracts are thin and papery. They are thorny woody, vines growing anywhere, its length about 1-12 meters tall, scrambling over other than plants with their hooked thorns. They are evergreen where rainfall occurs all the year, or deciduous if

there is a dry season. The leaves are alternate, simple ovate acuminate, 4-13 cm long. The actual flower of the plant is small and generally white but each cluster of three flowers are surrounded of three or six bracts with the bright colours associated with plant, including pink, magenta, purple, red orange, white or yellow[10]. The peak blooming time is September to December and again February to june but some cultivars like 'snow white' and 'snow queen' flower only once in winter[9]. *Bougainvillea glabra* choicy have been used by the traditional practitioner of Mandsaur in variety of disorders like diarrohea, reduce stomach acidity, cough and sore throught, decoction of dried flowers for blood vessels and leucorrohea and decoction of the stem in hepatitis. The main part used is leaves[11]. The reported constituents in leaf are alkaloids, flavanoids, tannins, saponononins and proteins[12]. The leaves of *Bougainvillea glabra* choicy are reported to have insecticidal activity[13], anti-inflammatory[8], antidiarroheal activity, anti-ulcer and anti-microbial activity[14], anti hyperglycemic activity[15].

This study was designed to examine the cardiotonic effects of *Bougainvillea glabra* another *Bougainvillea* species apart from B. *spectabilis* on Isolated frog heart (Syme's Technique) based on the glycosides present in the plant extracts.

MATERIALS AND METHODS

ANIMALS

Adult frogs of either sex weighing 200-250gms (*Rana tigrina*) were selected. All studies were performed in accordance with Institutional Animal Ethics Committee (IAEC NO: 439/PO/01/a/CPCSEA).

FLOWER COLLECTION AND AUTHENTICATION

The flowers of *Bougainvillea glabra* were collected from the botanical garden of K.J.R college of Pharmacy. The flowers were authenticated by Dr. D. Vijaya Bhima kumar, head of the department of Botany, Government Degree College Mandapeta, East Godavari (Dist). The flowers were dried under the shade for a few days and powdered.

PREPARATION OF EXTRACT

The powder material was subjected to maceration. The solvent used are water. The powder material of *Bougainvillea glabra* flowers were weighed and macerated in aqueous solvent for a period of 7 days with occasional stirring. The extracts were then concentrated by using Rota evaporator and were air dried at room temperature, weighed and percentage yield was calculated. The color and consistency of the extracts were noted.

EFFECTS OF EXTRACT ON FROG HEART PERFUSION BY SYME`S TECHNIQUE[16]

Frog (*Rana tigrina*) was stunned by head-blow using a steel road and pithed. The skin and abdomen were cut and opened. The pectoral girdle was cut using a bone cutter and pericardium was cut and removed. Syme`s cannula was connected to the reservoir of frog Ringers solution and introduced immediately into the Sinus venosus of the heart. The connecting blood vessels were cut and heart was isolated from the animal and mounted on to a stand. Heart was then covered with thin layer of cotton wool to prevent drying. Frog Ringer solution was used to wet the heart frequently to prevent drying. Heart was connected to Starling Heart lever and adjusted to mark on the smoked drum for recording the responses of the heart. The level of frog Ringer solution in the Syme's cannula was maintained by fixing a glass tube into the cork fixed to the reservoir (Marriott bottle) tightly. The heart was allowed to stabilize and when the heart rate and cardiac output were taken, the recordings were made on a slow rotating sooted drum, to which a sooted kymograph paper was affixed. The effect of aqueous extract of flowers of *Bougainvillea glabra* per *se* (in frog Ringer solution) and its fractions were studied on isolated perfused frog hearts. The parameters studied include the force of contraction, heart rate and cardiac output. Minimum 5 min time was allowed between the additions of samples per se (in frog Ringer solution). When a blocker was used, it was diluted with known amount of the frog Ringer solution in the syringe itself and added slowly. The heart Rate (HR), Cardiac Output (CO) and force of contraction were the parameter used for the study. The solutions of extracts were prepared in frog Ringer`s solutions and then centrifuged. No suspending agents were used. The heart was constantly moistened with frogs Ringer solutions from time to time.

INVESTIGATION ON ISOLATED HYPO DYNAMIC FROG HEART

An isolated from heart preparations as described under Syme`s technique was set up. Instead of one reservoir, two reservoirs each for ½ - calcium and full calcium were used. The levels in the reservoir were maintained constant, which was tested by connecting each of the reservoirs to the Syme`s cannula. Experiments were conducted

by rendering the frog heart hypo dynamic by letting into heart; frog Ringer`s solution containing half-calcium from another reservoir through Syme`s cannula. Force of contraction was monitored to give approximately half the magnitude of normal force of concentration.

RESULTS

The parameters studied included force of contraction (FC), heart rate (HR) and cardiac output (CO). There was dose-dependent increase in HR with the doses of 1mg to 100mg by the aqueous flower extract of *Bougainvillea glabra.* CO increased between the doses of 10mg to 100mg. The increase in FC is dose-dependent between 10 and 100mg. 100 µg of Timolol (TIM) inhibits the force of contraction of heart produced by 10mg of extract (Figure-1). Under the influence of hypo dynamic heart FC, HR and CO were varied. The HR was increased under the influence of increased doses of the extract between 10mg to 100mg and was dose dependent. The FC increases in dose dependent manner. There was dose-dependent increase in CO. Influence of TIM on the action of the extract is observed as is seen under control responses. Adrenaline (10 µg) and Digoxin (300 µg) produced dose-dependent increase HR and dose-dependent increase in CO and dose-dependent increase in FC (Figure-2).

DISCUSSION

Cardiac glycosides and catecholamine have been used as the main therapeutic drugs in the treatment of congestive cardiac failure[17]. However, the dangers of cardiac glycosides intoxication are well documented[18] and doubts have been expressed about their long term effectiveness. The use of catecholamine is limited by their in- sufficient differentiation between positive ionotropic and chronotropic action, their potential arrhythmogenic properties and tachyphylaxis due to receptor down regulation[17]. From the above observation we investigate cardiotonic principles in aqueous flower extracts of *Bougainvillea glabra* by different experimental methods. Study was conducted at different doses less than 10 mg Bougainvillea *glabra* aqueous extract doesn't show any cardiac stimulant and cardiotonic action on isolated frog's normal and hypodynamic heart. When the dose administered at 10 mg *Per se* (in frog half calcium Ringer solution) in normal heart it produce marginal stimulant action and shows very prominent dose dependent cardiac stimulant action with increase in heart rate and cardiac output, the action is blocked by the Timolol (beta blocker) thus indicates this action is mediated through β_1 receptors. In case of hypodynamic heart aqueous flower extract produce prominent increase in force of contraction (positive ionotropic effect) and increase in heart rate (positive chronotropic activity) and increase in cardiac output starts at 10 mg *Per se* (in frog half calcium Ringer solution) dose and it continued as dose dependent manner. This positive ionotropic effect is blocked by the Timolol a β blocker indicates that positive ionotropic effect is through β receptors. The effect of aqueous flower extract was compared with Adrenaline. Action of digoxin which is a standard cardiotonic agent, on hypodynamic heart is observed that it produces positive ionotropic effect and negative chronotropic effect.

CONCLUSION

Aqueous flower extract of *Bougainvillea glabra* elicited dose dependent positive ionotropic effect on normal and hypodynamic frog heart. This shows that *Bougainvillea glabra* produces cardiotonic activity. Timolol a non selective beta blocker block the responses produced by *Bougainvillea glabra* indicating that it may elicit the mechanism of action through β_1 receptors. Further evaluation is warranted to explore the possibility of mechanism of action and some more pharmacological actions for therapeutic gain of *Bougainvillea glabra* in future.

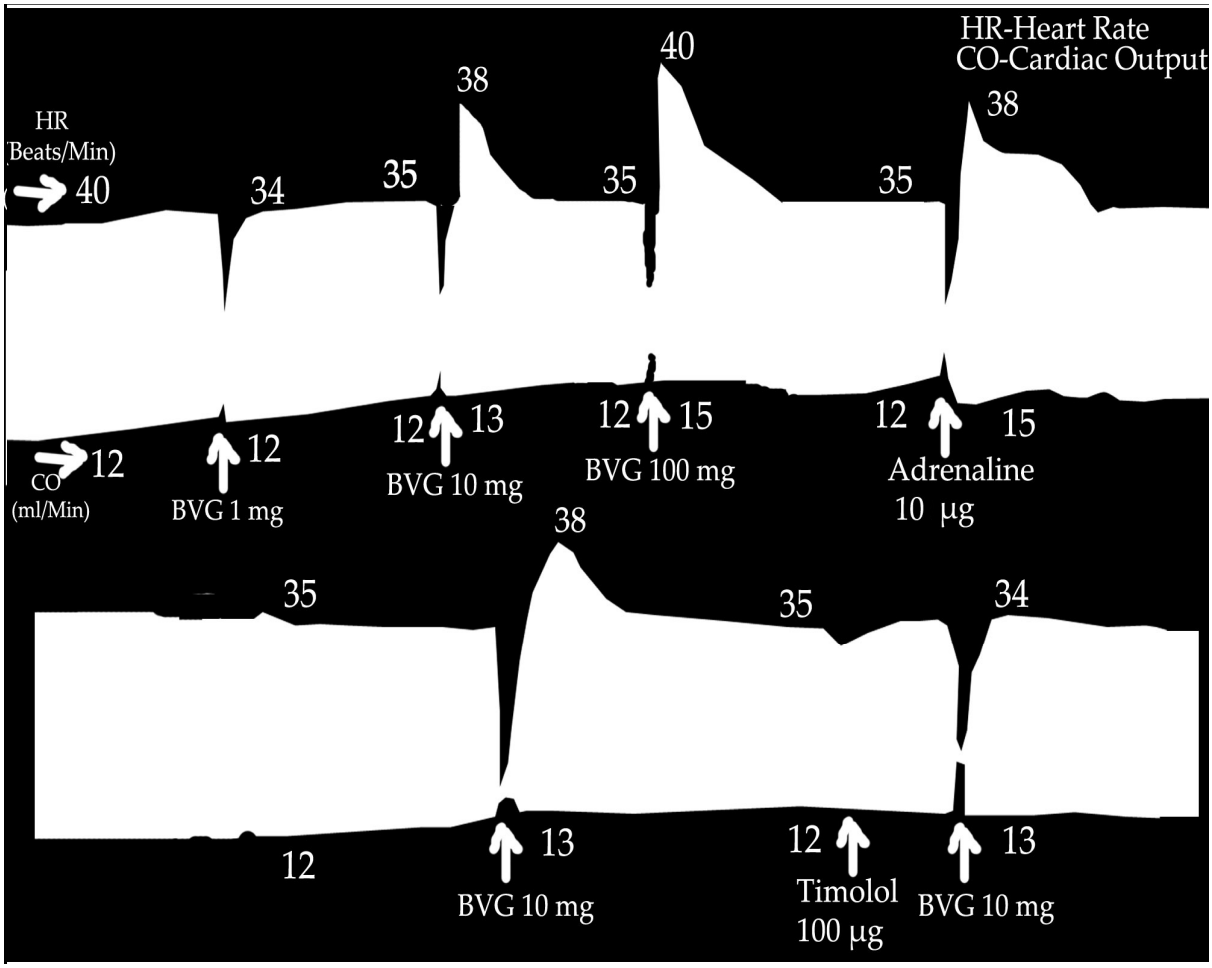

Fig. 1: Effect of aqueous flower extract of *Bougainvillea glabra* on isolated normal frog Heart

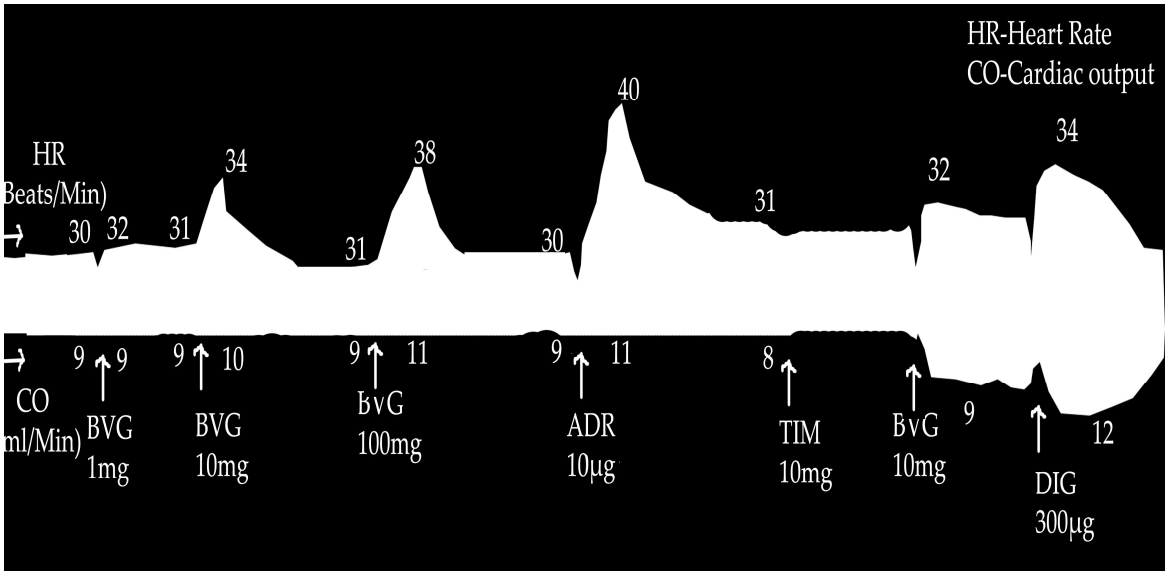

Fig. 2: Effect of aqueous flower extract of *Bougainvillea glabra* on Isolated Hypodynamic frog heart

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