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Research article

In-vivo evaluation of Anti-hemorrhagic potency of Siddha Medicine Kadukkai Chooranam

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ABSTRACT

Background: The kadukkai chooranam is a siddha medicine having the potency of strong astringent in nature in terms of taste. It is widely used for the treatment of bleeding disorders especially this drug combination is used for the treatment of dysfunctional uterine bleeding (Menorrhagia).

Aim: The aim of this study was to determine the effect of anti-haemorrhagic potency of Kadukkai chooranam in animal models.

Methedology: Wistar albino rats of either sex are randomized into four groups of six animals each. Group I received vehicle (1ml/kg; orally), Group II received Kadukkai chooranam drug at the dose of 100mg/kg; orally, Group III received Kadukkai chooranam drug at the dose of 200mg/kg; orally, Group IV served as standard Adrenochrome10µg/kg; orally. The animals were administered the test drug orally and the blood sample were collected periodically for valuation of clotting parameters like prothrombin time, clotting time, bleeding time etc.

Results: The present research work shows that, it enhances the Prothrombin time, Activated Partial Thromboplastin time and Fibrinogen time etc. 200mg/kg of kadukkai chooranam of thrombin time shows 22.21±0.78 when compared the standard 15.82±2.65 which is slightly lows. The action of the kadukkai chooranam is quite higher than the AC of standard drug.

Conclusion:

Based on the study report, we can conclude that, this drug formulation Kadukkai chooranam has greater potential of preventing haemorrhage related disorders and may be used for clinical management of haemorrhage, where in further clinical investigation/clinical studies are the future need.

Keywords:

Anti-styptic action, Anti-haemarrhogic activity, Terminalia chebula.

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INTRODUCTION

Recently there are lot of attraction towards natural based herbs as an antimicrobial agent because of its eco friendly and health hazardless nature. The traditional Indian systems of Ayurveda and Siddha medicines support the importance of medicinal plants to treat diseases. At the turn of the century, approximately 170 herbal drugs were officially recognized in the United stated Pharmacopea (U.S.P) and National Formulary (N.F)(Afshari et al., 2016). The Director of WHO Traditional Medicine reported in 1993 that 80% of the world population rely chiefly on traditional medicine, mainly plant based, specially for their primary health care needs. In India 70% of populations are reported using traditional medicine for primary health care. The present annual turnover of herbal medicinal products manufactured by large companies is estimated to be approximately US $ 300 million, compared to a turnover of approximately US $ 2.5 billion for modern drugs.

The drug kadukkai chooranam is mainly composed of Terminalia chebula and Adathoda vasica juice. *Terminalia chebula* is an important medicinal plant in Indian tradition and it is most frequently used herb in all the traditional medicines especially siddha system of medicine(Rubab and Ali, 2016). *Terminalia chebula* is a medium- to large-sized tree distributed throughout tropical and subtropical Asia, including China and Tibet. This tree is found in the forests of northern India, Uttar Pradesh and Bengal, and is common in Tamil Nadu, Karnataka and southern Maharastra. *Terminalia chebula* is commonly known as black myroblans in English, Kadukkai in tamil and harad in Hindi.

Terminalia chebula is routinely used as traditional medicine in the name of 'Kadukkaai' by tribal of Tamil Nadu in India to cure several ailments such as fever, cough, diarrhea, gastroenteritis, skin diseases, candidiasis, urinary tract infection and wound infections. It is a well known fact that the demand for the herbal drug treatment of various ailments is increasing and plant drugs from the siddha medicine system are being explored more, not only in India but also globally(Ratha and Joshi, 2013). Menorrhagia is one of the most common bleeding manifestation in women. Menorrhagia or bleeding which is excessive in amount and duration during menstruation is one of the gynaecological complaints in which out of 20-25% of women report suffering from it. One in 20 women aged between 30-50 (Maruthappan and Shree, 2010) were consulting a doctor each year with the complain and history of Menorrhagia. Causes of the condition include disorders of the blood that affects blood clotting, pelvic infections, fibroids, endometrial polyps, endometrial hyperplasia and even pelvic cancers. If there is no obvious cause Menorrhagia falls into category of Dysfunctional Uterine Bleeding (DUB). Heavy menstrual episodes may negatively (Ratha and Joshi, 2013) affect quality of life by limiting normal activities, social life and work of female population. Aim of this paper is to evaluate the anti-haemorrhagic potency of kadukkai chooranam in wistar rats(Maruthappan and Shree, 2010).

In *Terminalia chebula*, 33% of the total phytoconstituents are hydrolysable tannins (which may vary from 20-50%) and are responsible for pharmacological activity. These tannins contain phenolic carboxylic acid like gallic acid, ellagic acid, chebulic acid and gallotannins such as 1,6 di-*O*-galloyl-β-D-glucose, 3,4,6 tri-*O*-galloyl-β- D-glucose, 2,3,4,6 tetra-*O*-galloyl -β-D-glucose, 1,2,3,4,6 penta-*O*-galloyl-β-D-glucose(Manosroi et al., 2010). Ellagitannin such as punacalagin, casurarinin(Naik et al., 2004), corilagin and terchebulin and others such as chebulanin, neochebulinic acid, chebulagic acid(Naik et al., 2004) and chebulinic acid(Jokar et al., 2016a) reported in various researchers. The tannin content varies with the geological variation. Flavonol glycosides,(Jokar et al., 2016a) triterpenoids, coumarin conjugated with gallic acid called chebulin(Jokar et al., 2016b), as well as phenolic compounds(Bag et al., 2013) were present in this, which are the chief acting compounds responsible for the therapeutic actions.

MATERIALS AND METHODS

Kadukkai chooranam was taken from the literature Agathiyar attavanai vaagadam used to treat Dysfunctional Uterine Bleeding (Menorrhagia). This drug mainly composed of Terminalia chebula fruit rind and leaves of Justicia adathoda.

Plant material and authentication

The raw material Terminalia chebula and Adathodai leaves were purchased from a herbal laboratory/Traditional store. It was authenticated by botanical experts and used for the preparatory process.

Clinical usage of the research medicine

Fruit rind of 100 (Kadukkai) Terminalia chebula is grinded using fresh leaf juice of (Adathodai) Justicia adathoda and dried well.

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This procedure is repeated for 14 times. Adult human dose is 1gm thrice a day with honey from the first day of menstrual cycle upto bleeding stops with a regular review for each 7 days. The treatment is given for 3 consecutive cycles.

Animals for experimental studies

A total of four groups of 6 animals i.e 24 animals of either Female and male Wistar albino rats weighing 200 ± 10 g were used. The animals were housed six per cage maximum. Each animal at the commencement of its dosing should be between 8 and 12 weeks old and its weight should fall in an interval within±20 % of the mean weight of the animals. They were fed a normal commercial pellet diet; they were given water ad libitum and maintained under laboratory conditions (temperature 22-24°C, relative humidity 60-70%)(Cock, 2015). All the animals were divided into four groups of six animals each, acclimatized to the laboratory a week prior to the experiments. The experimental protocol was carried out according to the guidelines and approved by the Ethics Committee IAEC No: IAEC/XLIV/15/CLBMCP/2014.

Procedure

Wistar albino rats of either sex are randomized into four groups of six animals each as previously described. The animals were administered the test drug orally and the blood sample were collected periodically for valuation

- Group I - received vehicle (1ml/kg; orally)
- Group II- Kadukkai chooranam drug at the dose of 100mg/kg; orally
- Group III- received Kadukkai chooranam drug at the dose of 200mg/kg; orally
- Group IV- served as standard Adrenochrome10µg/kg; orally

Clotting time

The tail of the animal warmed for 1 min in water at 40°C, dried and cut at the tip with a razor blade. A 25 µl sample of capillary blood was collected into a micro-hematocrit glass capillary. The chronometer was started when the blood first made contact with the glass capillary tube. The blood left to flow by gravity between the two marks of the tube, 45 mm apart, by tilting the capillary tube alternately to +60° and -60° angles with respect to the horizontal plane until blood ceased to flow (reaction end point).

Bleeding time method (BT)

The tail of the rat warmed for 1min in water at 40°C and then dried. A small cut was made in the middle of the tail with a scalpel. Bleeding time started and noted when the first drop touched the circular filter paper and checked at 30 s intervals until bleeding stops.

Prothrombin time (PT)

0.1 ml of plasma mixed with 0.2 ml of pt reagent(calcium thromboplastin) maintain 37°C,and

absorbed the animals until formation of the fibrin clot. The time should be noted.

Activated Partial Thromboplastin time (APTT)

0.1 ml of plasma with 0.1mi of APTT reagent (cephalin-karolin suspension) incubated 37°C for 5minutes and then adds 0.1ml of 0.025ml $cacl_2$ solution, until formation of the fibrin clot visually detected. The time is noted.

Fibrinogen time

0.25ml of animal blood plasma add 0.05 ml of saline, and incubated 37°C. After 30's add 0.1ml ofstreptokinase solution, wait for 30's, then add 0.1mlof bovine thrombin added. Start the stopwatch. 30 are later which time the fibrinogen clot formed.

Statistical analysis

All the study statistical process was carried out through One-way ANOVA and followed Dunnet's test for multiple comparison between the groups.

RESULTS AND DISCUSSION

Effect of drug kadukkai chooranam of clotting parameters

The blood clotting profile of control and drug treated rats showed that, treatment with kadukkai chooranam in its dose of 100 and 200 mg/kg possess significant reduction in clotting profile time such as bleeding time ,clotting time, prothrombin time, activated partial thromboplastin time and fibrinogen time when compare to the control group of animals. But, Standard also slightly lowers in its range, when compared with the test drug. There is no such statistical significance was observed(Table 1). The Bleeding time and clotting time are almost same in all the treatments groups and the drug has slight potency when compared to AC illustrated in Figure 1. & 2. The fibrinogen level is slightly increased in the 100mg/kg and gradually decreased in 200mg/kg of kadukkai chooranam dose administration. This shows the potency of fibrinogen formation and its response to the styptic action.

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Table 1. Result of clotting parameters evaluated for the test drug

Parameter	Control	Kadukkai chooranam 100 mg	Kadukkai chooranam 200 mg	AC(10µg)
Bleeding time	81.22±1.33	93.33±1.12	88.74±2.77	84.34±3.23
Clotting time	118±2.43	116.3±1.65	110±2.31	101.32±1.31
Prothrombin time	26.11±1.44	24.65±1.23	22.65±1.87	20.08±1.54
Activated thrombo-plastin time	25.65±0.78	22.34±0.34	19.83±0.54	15.43±1.42
Thrombin time	32±1.74	26.55±1.23	22.21±0.78	15.82±2.65
Fibrinogen	190.5±2.11	178±1.90	150.4±2.21	123.43±1.25

N=6 ;Statistical analysis one way ANOVA followed by Dunnett t-test.

Figure 1. Cloting parameters analysed for this study

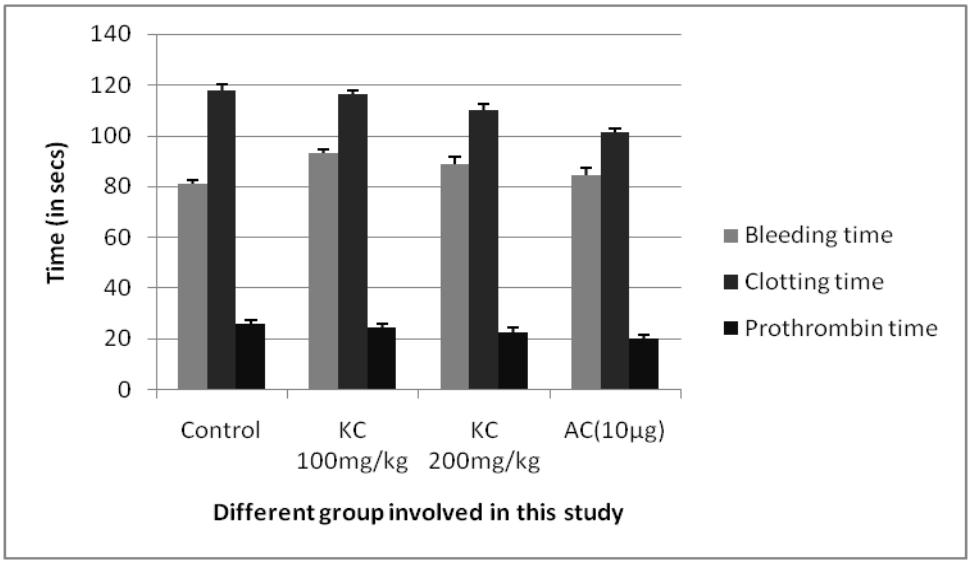


Figure 2. A-TP an Prothrombin time of Kadukkai chooranam

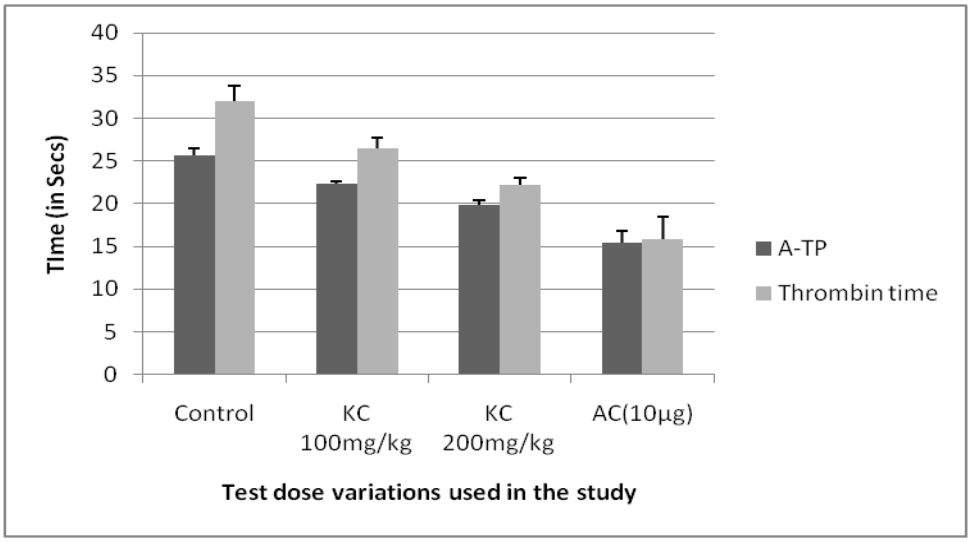
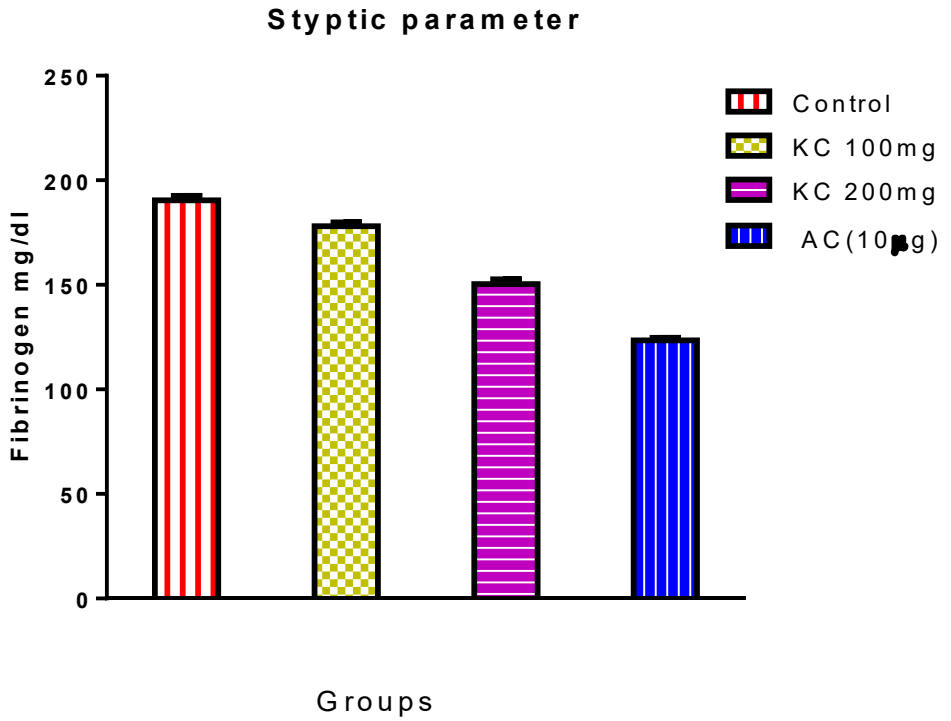


Figure . 3 Fibrinogen response for the drug kadukkai chooranam



CONCLUSION

The study suggesting that, the anti- haemorrhagic activity of the drug Kadukkai chooranam in 200mg/kg shows highest in its level and it can be used for the treatment of emergency and bleeding disorders. Haemorrhage is the main reason in the causes of death in 48 h after trauma, which accounts for 80% in all trauma accident. Early control of haemorrhage remains the most effective strategy for treating combat casualties. Catastrophic blood loss often results in hemorrhagic shock as demonstrated in animal models, resembling human outcomes. Therefore development of compounds to improve hemostasis and save patient's life in the trauma is of medical importance. Moreover, based on the literature, this drug kadukkai chooranam will be more useful to treat the gynaecological disorders. There is a dose dependent activity is seen in this study and significantly activity increased.

SOURCE OF FUNDING : Nil

CONFLICT OF INTEREST : None declared

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