Efficacy of Siddha drug KuruverKudineer for Anxiolytic activity by using Elevated plus maze method on Mice

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Abstract:

KuruverKudineer is a Siddha herbal formulation used for treating many disease especially Autism spectrum disorder (Mantha Sanni) for both Children and adults. Dealing with these facts many studies were to be carried out and here Anxiolytic activity is studied in detail. **Aim:** To evaluate the efficacy of Kuruverkudineer for Anxiolytic activity by using Elevated plus maze method on Mice. **Materials and Methods:** The pharmacological activity of KuruverKudineer was done in National Institute of siddha, Tambaram Sanatorium after the approval of Institutional Animal ethical committee. Animal experimentation was done on

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Swiss albino mice divided into 4 groups containing 6 mice per group. Anxiolytic activity was studied by using Elevated plus maze method. **Results and discussion:** Kuruverkudineershows satisfactorily good anxiolytic activity when compared to control and standard group. This siddha drug exibits anti-anxiety properties. Further study is required for scientific validation and to prove its clinical efficacy in multicentre clinical study.

Key words: Anxiolytic activity, elevated plus maze, KuruverKudineer, Swiss albino mice, Autism spectrum disorder, Mantha sanni.

Introduction:

Kuruverkudineer is a well known traditional Indian medicine which was widely used in the treatment of many clinical conditions in worldwide. It has various therapeutic actions such as antioxidant, anti depressant, anti anxiety, adaptogenic, immunomodulating ,anti bacterial, anti fungal , neuroprotective, cognitive enhancer etc.,It contains the essential oils like sesqueterpenes, sesqueterphenols and sesqueterphenones. The main chemical constituents are Vetiverol, Vetivone [7], Khusimone, Khusimol, Vetivene, Khositone, Terpenes, Benzoic acid,Tripene-4-ol, ß-Humulene, Epizizianal, vetivenylvetivenate, iso khusimol, Vetiver oils, vetivazulene. It is used for various kinds of disease and it is especially used as a nervine tonic. Considering these facts many scientific studies are to be carried out. Autism Spectrum Disorder (ASD) is more common in children now-a-days. It is a neuro disorder with confused state, socioemotional and depression and Anxiety etc. The traditional sasthric Siddha formulation KuruverKudineer is indicated for the management of Mantha sanni(ASD). Even though the formulation has been prescribed since long back, its necessary to evaluate the anxiolyticactivity of above said formulation.

Material and methods:

Preparation of experimental formulation

Kuruverkudineer as siddha herbal drug formulation was identified for this study. Raw drugs to prepare this medicine were purchased from the well reputed country shop in Tambaram. The raw materials were authentication from the department of Medicinal Botany, National Institute of Siddha, Chennai. After process the medicine was proper purification , the medicine was prepared in Gunapadam lab of NIS. The

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Prepared medicine was stored in glass container authenticated by the concerned guide for its completeness.

Vernacular/ Tamil name	Botanical Name	Parts Used	Part
Vettiver	*VettiverZaizanoids*	Root	1/4 palam
Vilamichu	*Plectranthusvettiveroids*	Root	1/4 palam
Chukku	*Zingiber officinalae*	Dried rhizome	1/4 palam
Parpadagam	*Hedyotiscorymbosa*	Root	1/4 palam
Siruthaeku	*Clerodendrumserratum*	Root	1/4 palam

Purification :

Vettiver*(Vettiverazizanoides)* :cut into a small pieces and dried at day time

Vilamichu*(Plectranthesvettiveroides)* : cut into a small pieces and dried at day time

Chukku (*Zingiber officinalae)* : Add 2 part of sunnakkal 1 part of Zingiber officinalae for 3 hours , wash it and then dried . After that external skin was peeled off.

Parpadagam*(Hedyotiscorymbosa)* : remove the dust materials then washed into pure water and then dried.

Sirutheakku*(Clerodendrumseratum)* : cut into a small pieces and dried at day time

Fig 1: Ingredients of experimental formulation

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Preparation method:

Ingredients mentioned above are made as a coarse powder and then soaked in a vessel containing of water 240ml boiled and reduced to 1/4th of its volume and filtered.

Pharmacological Activity (Anxiolytic study-Elevated plus maze method)

The pharmacological study protocol has got an approvalfrom Institutional ethical committee of National Institute of Siddha, Chennai (NIS/IAEC/-IV/04105012017).The Swiss albino Mice aged 6-8 weeks weight with 20-35g and both gender was Male and female were selected this study. The drug was administrated by oral route. The room temperature and humidity wasmaintained at 22+40-65%. Same sex of 3 animals was housed in propylene cages with husk bedding. Each animal has marked in picric acid on the fur for identification (Head, Neck, Body and Base of tail) and it was indicated in cage card along with the number. CPCSEA guidelines was strictly adhered. Animals would be monitored for health, food with adequate nutrition (Rodent pellets) and water atlibidum etc. for 24 x7 days per week. Animal husbandry would be 12-hour light and12-hour dark cycle. Polypropylene cages would be used with proper husk bedding. Animal excreta was disposed properly and monitored hygienic condition. All animals was observed for signs of illness, injury or abnormal behaviour treated with veterinary surgeon. If any animal die immediately post-mortem would done for observation of autopsy changes. Diseased animals would be monitored, treated and quarantined in the separate cages. After the experimental period, animals would be reutilized for another study followed by acclimation period or else would be leave independently.

Table1: Animals required for Pharmacological activity

S.No	Groups	No of animals(Both sex)
1	Group I- Vehicle control (Water)	6
2	Group II- Standard drug –Alprazolam (0.05ml/20-30 gram of mice)	6
3	Group III- Kuruver kudineer Dose I-0.4ml/20-30 gram mice	6
4	Group IV- Kuruver kudineer Dose I -0.3ml /20-30 gram mice	6
	Total no of animals required	24

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The Elevated plus maze has been described as simple method for assessing anxiety response of rodents. The apparatus used for the elevated plus maze test is in the configuration of a+ and comprises two arms (25*5*0.5cm) across from each other and perpendicular to two closed arms (25*5*16cm) with a centre platform (5*5*0.5 cm). The open arm have a very small (0.5cm) wall to decrease the number of fall, whereas the closed arms have a high (16cm) wall to enclose the arm. The entire apparatus is 50cm above the floor and is placed in empty circular tank to protect the mice that fall or attempt to escape during the experiment .The apparatus is made of plastic materials. The platform is white and the walls are transparent. There is a variation and colours of the apparatus of elevated plus maze.

The behaviour testing room is soundproof and the illumination level is maintained at 100 lux. A mouse is placed in the centre area of the maze in its head directed toward a closed arm. The elevated plus maze test is observed. The number of entries into each arm and the time spent in the open arms are recorded and these measurements serve as an index of anxiety like behaviour. Mice are allowed to move freely about the maze for 10 min. The distance travelled the number of entries into each arm, the time spent in each arm and the per cent of entries into the open arm are calculated. After each trial, all arms and the centre area are cleaned with super hypo chlorous water, that is an efficient odour removal agent and has relatively weak odour of itself compared to their cleaning solutions to prevent a bias based on olfactory cues.Thus we can conduct the tests under controlled condition regarding olfactory cues. A task using a y shaped apparatus that include an elevated open alley which produced a strong approach avoidance conflict an closed assay. The Mice demonstrated the most robust avoidance response in the first 5 min after placement in the elevated open alleys. The behaviour that are typically observed when rodents are in the elevated plus maze time spend and entries made on the open and closed arms. Antianxiety behaviour can be determined simultaneously with a measure of spontaneous motor activity and the arm entries made in the maximum of an optimal motor activity.

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Fig2: Elevated plus maze method

Results:

Table 2: Shows the results of KuruverKudineer effect in Mice

Average Calculation (n=6)				
	Open arm		**Closed arm**	
Control group	Number of entry	5	Number of entry	12
	Spent time	34sec	Spent time	1min56sec
	Open arm		**Closed arm**	
Standard group (Alprazolom IP)	Number of entry	8	Number of entry	11
	Spent time	1min7sec	Spent time	2min4sec
	Open arm		**Closed arm**	
Low Dose (Kuruver kudineer)	Number of entry	13	Number of entry	12
	Spent time	1min8sec	Spent time	2min5sec
	Open arm		**Closed arm**	
High Dose (Kuruverkudineer)	Number of entry	9	Number of entry	10
	Spent time	1min2sec	Spent time	2min9sec

Kuruverkudineer shows satisfactorily good anxiolytic activity when response compared to control and standard group. This siddha drug had definite anti-anxiety properties.

Discussion:

In General the preparation of drug is simple as well as economical. Based on the results obtained it is proved that this trial drug exhibits anti anxiety properties.The Global burden of Mantha sanni(Autism spectrum disorder), increasing prevalence and its impact in reducing the quality of life in children has prompted the author to choose an efficient and nutritive drug which is believed to good in central nervous system. KuruverKudineer has showed good response with no adverse effect, very effective and simple to administer.This has, in turn, provided a golden opportunity for new drug established in the management of Mantha sanni.Further study is required for scientific validation to prove its clinical efficacy in multicentre clinical study.

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