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Research article

Acute toxicity and sub-acute toxicity study of Siddha herbal formulation "*Jaathipalathi Chooranam*"

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Abstract

Background

Jaathipalathi chooranam (JPC) is Siddha poly herbal preparation, primarily composed of *Myristica fragrans(Linn).* In terms of Pharmacological action JPC ishaving significant bronchodilator (Nisha et.al,2017) antispasmodic, antidiabetic and hypolipidemic actions.(Arulmozhi et.al,2007). As per the reference text Gunapadamporutpanpunool, the indication of JPC is prescribed primarily for the management of Respiratory disease , DUB and Vatha diseases (Murugesa Mudhaliyar,2016).

Objective

To determine the acute and sub-acute toxicity effect of the siddha poly herbal formulation *Jaathipalathi Chooranam (JPC).*

Methods

Acute &sub-acute toxicity of *Jaathipalathi Chooranam* was evaluated *in* wistar rat models with oral administration of JPC 50mg/kgbw for seven days in acute and 20 days in subacute toxicity.All the studies were carried under OECD Guidelines.

Results

The *Jaathipalathi Chooranam* has not produced any acute and sub-acute toxicity symptoms, no changes in corporal weight and haematological parameters and hepatic enzymes like SGOT & SGPT . The result of the study suggests that JPC is safe to use for long term prescription.

Conclusion

The results suggested that *Jaathipalathi chooranam* is found to benon-toxic, when action of JPC was analyzed on hematopoietic and leucopoietic systems.

Keywords

Jaathipalathi chooranam, Siddha drug, Siddha medicine, Toxicity studies

Keywords: Siddha medicine, Munnailai kudineer, Rat models.

Introduction

The drug *Jaathipalathichooranam* is a poly herbal formulation, which has indicated for the treatment of *Swasakasam* (Bronchial asthma). It is a common and inflammatory disease, irreversible damages in bronchial tree. It is characterized by recurrent episode of wheezing, dry cough, chest tightness, and shortness of breath. These episodes may occur a few times a day or a few times per week.

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Depending on the person they may become worse at night or with exercise. Bronchial asthma is a very common disease in the society due to increasing exposure to air pollution and western life style. It is common in both sex but more prevalent among boys, while during adolescence and adulthood, it affects girls and women more. In 2025, expecting more than 300 million people were affected in worldwide. In future in India wills affected more than 100 million peoples have affected in this disease. It is one of the leading causes of morbidity and mortality in rural India (Smith 2000).

Materials and Methods

The *Jaathipalathi Chooranam (JPC)* is a good expectorant, antispasmodic action, Immuno-modulator, Bronchodilator (Nisha et.al,2017), Anti-oxidant, Anti- hyperlipedemic, Anti-diabetes actions(Arulmozhiet.al,2007). It was mentioned in*Sarabendhra Vaithiya Muraikal- Kasa Swasa Roga Sikicha Siddha text book .(pg.no:131,132) Mr.K.Vasudevasasthri, Dr.S.Venkadarajan, L.I.M.(Retd.),year of edition-2006.*

The study was carried out in the Department of Pharmacology with the approval of the Institutional Animal Ethics Committee, IAEC/R.SUBASHINI/TNMGRMU/MD (S)/321611009/KMCP/28/
2018 KM College, Tamilnadu

Collection of raw drug

The raw drug of *Jaathipalathi Chooranam* was purchased from Nagercoil based medical shop and authenticated by Medicinal Botanist &Gunapadam experts at Govt. Siddha Medical College, Palayamkottai-627002.

Animal Studies

Healthy adult male and female Wistar albino rat weighing between 170-200 g were used in this study. The animals were feed normal water and *ad libitum*. All the animals were acclimatized to the laboratory for 7 days prior to the start of the study. Acute oral toxicity of *Jaathipalathi chooranam* is carried out as per OECD -423 guidelines. After the ethical clearance from Institutional Animal Ethics Committee (KMCP/28/1.5.18).Determination of acute oral toxicity is usually the initial screening step in the assessment and evaluation of the toxic characteristics of all compounds. Acute toxicity is involved in estimation of LD_{50} (Shetty Akhila, *et al.*2007).

Acute toxicity study on female wistar rats

The wistar rat were put on fast over night and provided only water, after which the *Jaathipalathi chooranam* is administered orally50 $mg.kg^{-1}$ body weight in Tween-80. The animals are then observed for 14 days and maintained with normal food. A mortality rate of 2 or 3 animals in 14 days is recorded and the dose is said to be toxic dose. But when mortality of one animal is observed, then the same dose is repeated again for confirmation. However, if mortality is not observed, the procedure is repeated for further higher doses such as 300 and 2,000 $mg.kg^{-1}$ body weight. Any occurrences of toxic symptoms were observed for 72 hrs (Shah Ayub, 1997, Bürger, 2005). All test animals were subjected to gross necropsy.

Sub-acute test for Jaathipalathi chooranam(JPC)

This experiment evaluates thesub-acute toxicity potential of *JJaathipalathi chooranam*. Male and female Wistar rats weighing 180 ± 10 g were used in this study. The animals were divided into five groups of six animals each. The Group I were administered with a single daily dose of 0.5 ml of Tween 80 orally for 20 days. The animals in Group II werea dministered with 50 $mg.kg^{-1}$b.w. of the *JPC* orally once daily for 20 days. The animals in Group III were administered with 100 $mg.kg^{-1}$b.w. of the *JPC* orally once daily for 20 days. The animals in Group IV and V were administered once daily with 200 and 400 $mg.kg^{-1}$b.w. for 20 days (Pieme,*et al* 2006, Joshi, *et al* 2007, Mythilypriya, *et al.,* 2007). The animals were then weighed every five days, from initial day of the treatment, to record the weight variation. The collected blood samples wasanalyzed in lipids,renal profiles and hepatic enzymes.

Drugs	Botanical Name and family	Part used	Quantity
Jathikkai	***Myristicafragrans.Linn Myristicaceae***	Seed	Equal ratio
Kirambu	***Syzygiumaromaticum.Linn Myrtaceae***	Flower bud	Equal ratio
Cheviyam	***Piper nigrum.Linn Piperacea***	Root	Equal ratio
Sirunagappu	***Mesuanaggesarium.Linn Clusiaceae***	Flower	Equal ratio
Vellilothrappattai	***Symplocosracemosa.Roxb Symplocaceae***	Stem bark	Equal ratio
Thakkolam	***Illiciumverum.Hook Illicium***	Fruit	Equal ratio
Milagu	***Piper nigum.Linn Piperaceae***	Fruit	Equal ratio
Karpporam	***Cinnamomumcamphora.Linn Lauraceae***	Extract	Equal ratio
Nattusarkarai	***Sacharumofficinarum.Linn Poaceae***	Stem Juice	Qs

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Table 1. Acute Toxicity Study of *Jaathipalathi chooranam*

Treatment	Dose ($Mg.Kg^{-1}$)	Sign Of Toxicity ($St.Nb^{-1}$)	Mortality ($D.S^{-1}$)
Group I	0	0/3	0/3
Group II	300	0/3	0/3
Group III	2000	0/3	0/3

ST- Sign of toxicity; NB- Normal Behaviour; D- Died; S- Survive.

Values are expressed as number of animals (n=3).

Table.2.The effects of *Jaathipalathi chooranam* on body weight changes in rats

Treatment	Day 1	Day 5	Day 10	Day 20
Control	184.15±6.8	184.45 ±6.20	196.15 ±6.35	197.7±6.58
JPC **50 $mg.kg^{-1}$**	191.30 ±6.4	190.30 ±6.30	198.25 ±6.70	199.30±6.72*
JPC **100 $mg.kg^{-1}$**	183.35 ±5.7	186.30 ±6.40	196.55 ±7.10	198.36±6.30*
JPC **200 $mg.kg^{-1}$**	192.30 ±7.2	195.15±6.50	198.90 ±7.20**	207.45±7.26**
JPC **400 $mg.kg^{-1}$**	184.65 ±6.05	189.15 ±5.60	195.60 ±6.35**	208.66±7.38**

Table: 3 The effects of *Jaathipalathi chooranam* on kidney, heart, liver and brain of the rats

Treatment	Heart (gms)	Kidney (gms)	Liver (gms)	Brain (gms)
Control	0.340± 0.05	0.60± 0.03	3.32± 0.05	0.67± 0.05
JPC 50 $mg.kg^{-1}$	0.31± 0.02	0.74± 0.03	3.44± 0.03	0.70± 0.3
JPC 100 $mg.kg^{-1}$	0.32± 0.06	0.82± 0.04	3.36±0.02	0.68± 0.2
JPC 200 $mg.kg^{-1}$	0.31± 0.04	0.77± 0.02	3.34± 0.02	0.75± 0.05
JPC 400 $mg.kg^{-1}$	0.30± 0.03	0.78± 0.03	3.37± 0.03	0.77± 0.05

The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV, and V. The statistical analysis was carried out using one way ANOVA method, where **P<0.01.

Table.4.The Effect of *Jaathipalathi Chooranam* on Biochemical Parameters Such as Glucose, Cholesterol, Tri-glyceride, HDL and LDL.

Treatment	Glucose ($mg.dl^{-1}$)	Cholesterol ($mg.dl^{-1}$)	Triglyceride ($mg.dl^{-1}$)	HDL ($mg.dl^{-1}$)	LDL ($mg.dl^{-1}$)
Control	94.65± 0.62	40.62± 0.56	25.25± 0.45	135.25± 0.55	84.15±1.72
JPC 50 $mg.kg^{-1}$	92.50± 0.56	26.85± 0.25*	10.22± 0.23*	175.28± 0.65*	71.59±1.28
JPC 100 $mg.kg^{-1}$	89.45± 0.47	27.74± 0.26*	12.42± 0.28*	165.18±0.78*	69.84±1.10
JPC 200 $mg.kg^{-1}$	90.25± 0.55**	34.18± 0.30	14.84± 0.38*	184.30± 0.84*	48.60±1.30
JPC 400 $mg.kg^{-1}$	86.25± 0.45**	33.78± 0.28	16.28± 0.34*	182.2± 0.85*	46.50±0.84

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Table.5.The effects of *Jaathipalathichooranam* on biochemical parameters such as AST, ALT, ALP, TP and Albumin in rats

Treatment	AST ($IU.l^{-1}$)	ALT ($IU.l^{-1}$)	ALP ($IU.l^{-1}$)	TP ($g.l^{-1}$)	ALBUMIN ($g.l^{-1}$)
Control	331.5±12.40	67.5± 3.18	246.58± 8.80	69.85± 3.32	39.15±2.35
JPC 50 $mg.kg^{-1}$	320.0±9.50**	65.5± 2.20**	259.10± 2.75**	70.30± 2.32	36.30±2.65
JPC 100 $mg.kg^{-1}$	321.3±7.20**	63.1± 3.15**	253.18± 6.70**	80.15± 2.82	38.30±3.05
JPC 200 $mg.kg^{-1}$	316.4±7.95	58.4± 2.90	258.00± 5.20	69.25± 3.32	40.20±2.75
JPC 400 $mg.kg^{-1}$	326.2± 8.20	60.3± 3.52	262.40± 4.40	74.05± 2.58	39.48±2.70

Table.6.The effect of HB, Calcium, RBC and WBC in rats

Treatment	Haemoglobin ($mg.dl^{-1}$)	RBC (10^6 /mm^3)	WBC (10^6 /mm^3)	Calcium ($mg.dl^{-1}$)
Control	11.3± 0.25	9.15± 0.02	11.45± 0.05	9.45 ±0.02
JPC 50 $mg.kg^{-1}$	12.5± 0.26*	9.45± 0.04*	10.01± 0.01*	9.16 ±0.02
JPC 100 $mg.kg^{-1}$	12.3± 0.15*	9.55± 0.02*	8.35± 0.32*	9.27 ±0.20
JPC 200 $mg.kg^{-1}$	10.7± 0.20*	8.33± 0.12*	11.45± 0.03*	9.61 ±0.13
JPC 400 $mg.kg^{-1}$	11.5± 0.35*	8.51± 0.45*	10.55±0.13	9.75±0.02

Results

Acute toxicity study of *Jaathipalathichooranam* has showed no mortality or morbidity inover 15-days of period following single oral administration (Table-1). The animals did not showed any changes in the general appearance, physiological and pathological changes (Table no .1) when the trial drug was administered at the dose of 2000 mg/kg/bw.so the LD50 of Jaathipalathichooranam was taken as2000 mg/kg/bw.

The effects on body weight changes in rats

The effect of *Jaathipalathichooranam(JPC)* on the body weight changes of rat models were noted .from the study it was observed that, there was significant increase ($p<0.05$) in body weight in all the animals observed. The results are shown in Table.2. A study on the effects of *Jaathipalathichooranam*on body weight changes in rats was carried out. The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV, and V. The statistical analysis was carried out using one way ANOVA method, where **P<0.01 *P<0.05.

The effects on kidney, heart, liver and brain of the rats

The effects of *Jaathipalathichooranam*on kidney, heart, liver and brain of the rats were observed. From the study it was clear that, significant ($p<0.01$) changes in the weights of various organs of the animals occurred with higher doses of the extract (400 $mg.kg^{-1}$bwt), Macroscopic examinations did not show any changes in colour of the organs of the treated animals compared with the control. The results are shown in Table.3. The study on the effects of *Jaathipalathichooranam*on kidney, heart, liver and brain of the rats was tested. The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV, and V. The statistical analysis was carried out using one way ANOVA method, where **P<0.01.

Effect of Jaathipalathichooranamon biochemical profiles

The effect of *Jaathipalathichooranam*on various biochemical value showed a significant decrease ($p<0.05$) in the plasma glucose level at higher dose (400 $mg.kg^{-1}$) compared with control rats. Significant decrease ($p<0.05$) in the plasma total cholesterol (TC), triglyceride (TG) and LDL-cholesterol levels. But a significant increase ($p<0.05$) in HDL-cholesterol levels were observed in treated animals, it was compared with control groups. AST, ALT and ALP levels were also normal in the *JPC* treated animals. such as glucose, cholesterol, triglyceride, HDL and LDL in rats was tested where, group I animals (GPI) The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV, and V. The statistical analysis was carried out using one way ANOVA method, where **P<0.01 *P<0.05 (Table no4.).

Changes in hepatic enzymes.

According to Table no 5 showed no elevation in hepatic enzymes level. The group I animals (GPI) were treated with normal saline ($5ml.kg^{-1}$), group II animals (GPII) with 50 $mg.kg^{-1}$ of HAEBD group III animals (GPIII) with 100 $mg.kg^{-1}$ of *Jaathipalathichooranam*, group IV animals (GPIV) with 200 $mg.kg^{-1}$ of *Jaathipalathichooranam*, and group V animals (GPV) with 400 mg.kg*Jaathipalathichooranam.* The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV, and V. The statistical analysis was carried out using one way ANOVA method, where **P<0.01 *P<0.05.

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Effect of *Jaathipalathi chooranamon* haematological parameters in rats

The effects of *JPC* observed for its effect on hematological parameter on the experimental rats. From the study it was evident that, a significant increase ($p<0.01$) were observed in the hemoglobin contents and RBC count in the group treated with 200 $mg.kg^{-1}$ body weight of *JPC* and a significant decrease of the parameters occurred in the group treated with 400 $mg.kg^{-1}$b.w.t compared with the control. There was no significant change in the calcium level in all the treated animals compared to the control (Table no.6). The statistical analysis was carried out using one way ANOVA method, where *$P<0.05$.

Discussion

The evaluation of acute and sub-acute toxicity in experimental animals is relevant in determining the overall toxicity of the herbal preparation. The acute toxicity study of *JPC* was not produced at the dose of 2000 mg/kg/bw. Hence, $1/10^{th}$ of 2000 $mg.kg^{-1}$ i.e. 200 $mg.kg^{-1}$ of dose was selected as a minimum dose for sub-acute toxicity study (Abu Taha Nael, *et al.,* 2008).(8). The result of sub-acute toxicity study shows that there was no significant change in animal behavior due to the absence of toxicity. The animals treated with *JPC* had normal growth pattern and body weight when compared with control rats treated with normal saline. The *JPC* at all concentrations do not produce liver damage. There were no significant changes in the hematological parameters between control and treated groups even when *JPC* was administered with higher dose of 400 $mg.kg^{-1}$.

Conclusion

According to the present study report JPCis non-toxic &safer to use in long duration. While concluding the biochemical and Liver enzymes study reports, no evidence of severe toxicity was associated with the administration of higher concentration of *Jaathipalathi chooranam*.

Conflict of Interest: Nil
Source of funding: Nil

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