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Physiochemical Analysis, Antipyretic and Anti-Inflammatory Potential of Kanakasava

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KEYWORDS
Kanakasav, Fever, and Inflammation

ABSTRACT:
Kanakasav is recommended in Ayurveda to cure inflammatory disorders so in present study physiochemical properties along with antipyretic and anti-inflammatory potential of Kanakasava was studied. Kanakasava was prepared according to Ayurvedic formulary. Kanakasava was administered orally to wistar albino rats to study acute toxicity. The antipyretic activity was evaluated by using Brewer's yeast-induced pyrexia model in rats, and anti-inflammatory activity was evaluated in the carrageenan-induced paw edema model in wistar albino rats.The findings showed that Kanakasav physiochemical parameters was in accordance with Ayurvedic Pharmacopoeia monograph and it contains active secondary metabolites such as alkaloids,flavonoids,Phenolics etc. Quantitative HPTLC showed that Kanakasav contain significant quantity of Quercetin.
Moreover,the results of an acute toxicity test showed no mortality in dose up to 10ml/kg. Kanakasav has possess remarkable anti-inflammatory and antipyretic potential. So, in future it may be use as safer alternative to synthetic drugs.

Introduction

Even these days, the ayurveda has taken its important place as an alternative medicine due to non-toxic and non-invasive nature. (Yadav et al., 2017) The ayurvedic medicines are classified in various categories such as Asava and Aristha, Lauha, Bati, Avaleha, Ghrita, Parpati, Taila, Guggulu, Churna and Rasa.(Jayaweera, 2022) Various methods are used to formulate ayurvedic medicines and among them fermentation is one of the methods used for the preparation of medicines. (Sayyad, 2012) Indian Ayurveda holds significant position due to two widely used fermented traditional medicines i.e., Arishtas (made from decoctions of herbal remedies) and Asava (made from powdered herbal drugs) (Vador *et al.*, 2012)

The powerful and less toxic dose forms with quick absorption include Asava and Aristha. 2019 (Das&Das) Astanga Hridaya, Asavarishta Sangragam, Astanga Sangraham, Bhaisajya Ratnavali, Charaka Samhita,Sushruta Samhita, Sarangadhara Samhita andYoga ratnagaram. These books discussed about Asava and Aristha in ayurveda. Asava and Aristha are the alcoholic preparations prepared by fermenting the juices or decoctions with the addition of sugar.(Chaudhary et al., 2011) The total products of asava and aristha are 79,out of which asava has 37 products and aristha has 42 products.(Maithanietal.,2019)Some of the common products of asava are Drakshasava, Kanakasava, Kumaryasava,Lohasava and Ushirasava and few pr important examples of aristha are

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Abhayarishta,Asokarishta,Babbularishta and Ashvagandhadyarishta.Asava and Arishtas are medications that are created by soaking the medications in a solution of brown sugar for a period of time while they undergo fermentation process that results in alcohol that makes it easier to extract the medicines' active ingredients. The medications may be in the form of a broth (kashaya)
or a coarse powder. This method also produces alcohol that acts as a preservative (Abad-Gil et al.,
2021). There are traditional guidelines for the fermentation-based manufacture of Ayurveda medicines, (Sabu&Haridas, 2015) Kanakasav is recommended in Ayurveda for various medicinal properties (AbhilashSV&SubrahmanyaP,2022). Itis an antiasthmatic formulation (Arora etal., 2017).

Resources and techniques:
Kanakasava test samples-The Kanakasava test sample were made in accordance with the Indian Ayurveda Pharmacopoeia.

Table:1 Formulation Composition:

S.no.	Ingredients	Botanical name	Quantity	Property
1	Kanaka (Dhatura)	*Datura metel*	192g	Analgesis and Antiinflammatory(Soni etal.,2012)
2	Vrsamula (Vasa)	*Adhatoda vasica*	192g	Vasicine and vasicinone are proven bronchodilators
3	Madhuka (Yasti)	*Glycyrrhiza glabra*	96g	Respiratory and Digestive disorders
4	Magadhi (Pippali)	*Piper longum*	96g	Managing coughand cold
5	Vyaghri (Kantakari)	*Solanum xanthocarpum*	96g	Respiratory problems Like cough and asthma
6	Kesara (Nagakesara)	*Mesua ferrea*	96g	Beneficial in relieving cold and cough as it removesExcess mucus from the lungs.
7	Visvabhesaja (sunthi)	*Zingiber officinale*	96g	Beneficial in reducing joint painand inflammation
8	Bharngi	*Clerodendrum serratum*	96g	Treatment of common cold
9	Talisapatra	*Abies webbiana*	96g	Carminative
10	Dhataki	*Woodfordia fruticosa*	768g	Good for throat
11	Draksa	*Vitis vinifera*	960g	Chronic Constipation
12	Jala	Water	24.576 L	Common cold
13	Sarkara	Sugar	4.8kg	Decreases Swelling
14	Ksaudra(Madhu)	Honey	2.4kg	Sweetening agent

Physicochemical studies-The following physicochemical properties of Kanakasava wasstudied (*Mushtaq etal*., 2020)

Organoleptic Properties-Kanakasava's organoleptic characteristics, including colour, odour, taste, and appearance, were examined. (Celik et al.2006)

Color :
The formulation (5 ml) was taken into petridish and placed in white background. It was studied for its color by naked eye.

Odor
The formulation (2 ml) was smelled patiently. The time interval between two smelling was kept 5 minutes to nullify the previous sensation.

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Taste:
The formulation (a teaspoon) was taken and examined for its sensation on taste buds of the tongue. The time interval among attempts was kept about 10 min., so as to makethe taste buds available fresh every time.

pH- The pH of the formulation was determined using a calibrated pH meter. pH was noted for Kanakasava after opening the bottle for seventh day and fourteenth day after opening the bottle (Yu&Ng,2002)

Alchol/Ethanol Content- The ethanol content was determined by testing 25 ml of test sample in500ml of RBF which is diluted with 150 ml of distilled water (round-bottom flask). A 100ml volumetric flask was filled with 90 ml of distillate, which was then diluted with distilled water. Moreover,the relative density was calculated, and the alcohol concentration was assessed.(Maithani and others, 2019).

Total Solid Content-The solid content of the formulation was assessed by heating a porcelain evaporator dish containing 10 ml of test sample on an e water bath at about 60–70°C.After that, the test sample washeated in oven at about 105°C to constant weight and dried under oven. The total solid content calculated in percentage w/v basis. (Benbelkacem et al., 2015) The results have been shown in Table 2

Density-Density of sample was determined by using pycknometer and results are shown in Table 2.

Surface tension.Surface tensions of sample was determined by using Stalagnometer (Subrahmanyam, 1997)and shown in Table 2.

Phytochemical Screening It was performed for evaluation of secondary metabolite in the sample

4.0 Quantative HPTLC Studies: HPTLC Studies Conducted on Kanakasav shows presence of Quercetin

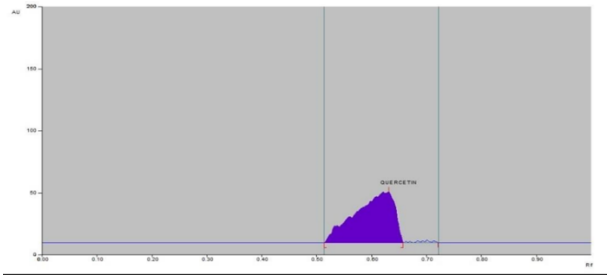

Fig.1 HPTLC Chromatogram of Kanakasav Showing presence of Quercetin

Table 2: Physicochemical properties of Kanakasava

S/N	Physicochemical Parameters	Observations
1.	**Description:-**	
	Colour	Dark yellow
	Odour	Aromatic
	Taste Appearance	Acrid taste
2.	pH	3.71 - 1.40
3.	Alcohol content(%v/v)	14 - 1.54
4.	Total solid content(%w/v)	19.70 - 1.23
5.	Density (gm/cm^3)	1.06- 0.30
6.	Surface tension	
7.	(dynes/cm)	58.01 - 0.82
8.	Phytochemicals	
	Present	Alkaloids, Flavonoids, Phenolics, Carbohydrates
9.	HPTLC Studies	Presence of Quercetin

Drugs and Chemical
The drugs namely, Indomethacin and Paracetamol (Calpol), and chemicals such as methanol(CDH)were used during the experimental study.

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Animals

For experiments, 150–200 gm Wistar albino rats were housed in the animal home of IFTM University, Moradabad, Uttar Pradesh, India. Every animal was securely housed in hygienic polypropylene cages with a constant temperature of 22 ± 1°C and light and dark cycles that alternated every 12 hours. The animals were fed a balanced diet of standard pellets (Hindustan Lever Ltd., India) and allowed unrestricted access to water. The CPCSEA criteria were agreed upon by the Institutional Animal Ethical Committee (IAEC, reference number IAEC/2021/33) and all experiment protocols and procedures were duly authorised.

Studies on Acute Toxicity

The acute toxicity was carried out in accordance with OECD 423 recommendations. For the toxicity testing, unisex albino rats were chosen. The acute experimental method was performed on the animals after an overnight fast. Rats were administered the extract orally at dosages of 1.25, 2.25, 5, and 10 mL/kg body weight. The animals were continually monitored for the first four hours following dosage for behavioral changes and for death at the end of 24hours. (Buschmann, 2013)

No signs of toxicity were observed in Kanakasav treated animals.

Kanakasav's anti-inflammatory properties in rat paw edema caused by carrageenan

A two-way ANOVA revealed that Kanakasav significantly reduced inflammation caused by carrageenan. Paw edema was inhibited in a time- and dose-dependent manner by Kanakasav. When compared to vehicle control rats, kanakasav (200ml/kg) demonstrated time-dependent suppression ($P<0.05$ and $P<0.001$ at 3h and 5h) of their increase in paw volume. As evidenced by a higher percent suppression of paw oedema in comparison to control rats, the high dose of Kanakasav (400ml/kg) demonstrated significant [($P<0.01$(3 h)and $P<0.001$(5 h)] inhibition of the mean rise in paw volume (edema) in a time-dependent manner. From 3 hours forward, the standard medication indomethacin also showed a comparable impact ($P<0.001$). The significant anti-inflammatory effect was observed following the injection of carrageenan.(Ramachandran S.2011)

Table:3 Anti-Inflammatory Effect of Kanakasava on Carrageen induced rat Paw oedema

Treatment	Dose(ml/kg)	Mean increase in paw volume (ml)		
		1 h	2 h	3 h
Control	-	0.281 ± 0.009	0.621 ± 0.015	0.821± 0.045
Kanakasav Low	200	0.256 ± 0.054	0.466 ± 0.043*	0.494 ± 0.036**
Kanakasav High	400	0.221 ± 0.032	0.441 ± 0.052**	0.456 ± 0.070***
Indomethacin	100	0.214 ± 0.036	0.334 ± 0.041***	0.334 ± 0.049***

Results are expressed as mean±SEM (n=5).*P<0.05;**P<0.01;***P<0.001 compared to Control

Antipyretic activity

Rats that were given Brewer's yeast-induced pyrexia model were used to assess the antipyretic efficacy. A digital thermometer was used to take the initial rectal temperature before pyrexia was induced. By injecting 15% Brewer's yeast (10 ml/kg body weight) in 0.5% w/v in distilled water subcutaneously, pyrexia was produced. Following an 18-hour yeast injection, rats exhibiting a temperature increase of more than 0.5 °C were identified. Subsequently, 25 rats were randomly assigned to four groups, each including five rats. A 15% oral suspension of yeast in distilled water was given to the control group. In the trial, paracetamol (100 mg/kg) was administered orally as the reference standard medication, whilst 200 and 400 mg/kg of Kanakasav were supplied orally. For every group, the rectal temperature was recorded at 0, 1, 2, 3, and 4 hours.. **(**Aiyalu R**,** 2010, Nisar M 2008)

Table: 4 Antipyretic effect of Kanakasav

Treatment	Dose(ml/kg)	Rectal temperature(F)				
		0 h	1 h	2h	3h	4h

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Control	-	98.56 ± 0.16	101.31 ± 0.25	101.44 ± 0.45	101.56 ± 0.22	101.46 ± 0.18
Kanakasav Low	200	98.97 ± 0.54	101.42± 0.40	101.66 ± 0.56	100.10 ± 0.46*	99.70 ± 0.30**
Kanakasav High	400	98.80 ± 0.20	101.47 ± 0.31	100.18± 0.24	99.96 ± 0.55**	99.28 ± 0.36***
Paracetamol	100	98.21 ± 0.29	101.79 ± 0.51	99.43 ± 0.26**	98.38 ± 0.60***	98.77 ± 0.37***

Results are expressed as mean±SEM (n=5).*P <0.05;**P <0.01;***P <0.001compared to control.

Result and Discussion

Physiochemical properties of Kanakasav are shown in Table 2 which are in accordance with Ayurvedic Pharmacopeia of India. Inflammation is a biological immunological reaction that may be produced by a range of reasons such as infections, damaged cells, and toxic substances (Chen et al., 2018) The immune system's primary goal is to rid the body of alien or non-self-cellular material including bacteria, viruses,fungus, parasites, and damaged cells (Bennett et al., 2018) It should be mentioned that the term "natural anti-inflammatory" refers to natural substances, as well as a person's lifestyle, exercise, and sleeping and eating habits (Ghasemian et al., 2016) It is generally known that pharmaceutical companies all over the world are interested in producing safer and more effective pain and inflammatory medications. Conclusively Kanakasav is proved to be anti-inflammatory and antipyretic agent.(Table 3 and 4) Activity may be present due to presence of various secondary metabolites and due to presence of Quercetin in significant amount as shown by HPTLC studies.So it may be use as safer alternative to synthetic drugs.

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