Effect of Potentized Homeopathic Preparations in Yeast Induced Pyrexia In Laboratory Animals

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Summary

The present investigation was designed to elucidate the anti pyretic activity of various homeopathic preparations viz. Aconite, Arnica, Atropa, Conium, Ferrum phosphoricum, Pyrogenium. All the preparations were administered at clinically prescribed doses of 6c, 12c, 30c, 200c, 1M to the male wistar rats after inducing pyrexia by sub cutaneous injection of yeast. The other experimental groups consisted of animals treated with distilled water, succussed distilled water, dispensing alcohol, succussed dispensing alcohol, and paracetamol (150mg/kg p.o.). The temperature was monitored at 0, 30, 60, 90, 120, 150, 180 minutes and 24 hours after the administration of the various homeopathic preparations and vehicle. Conium at the doses of 30c, 200c, and 1M there was able to significantly inhibit rise in rectal temperature in a dose dependent manner. The rectal temperature in all the animals treated with Aconite, Arnica, Belladona, and Pyrogenium did not show any fall with respect to time when compared with the vehicle treated group of animals.

Keywords: Homeopathic preparations, pyrexia, animals

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Introduction

Pyrexia is characterized by elevation of body temperature due to a plethora of substances collectively called pyrogens[1].These substances lead to elevation in the levels of prostaglandins which reset the temperature regulation centre at the hypothalamus. Fever is an elevation of body temperature that exceeds the normal daily variation[2]. Once the hypothalamic set point is raised, neurons in the vasomotor center are activated leading to vasoconstriction. Generally, the temperature increases by 1^0 to 2^0C. Few physiological changes occour such as shivering and increased heat production by liver[3]. An array of homeopathic medications are prescribed by the physicians but there is a severe paucity of scientific data to provide scientific credence to the retrospectively elucidate the effect in laboratory animals. Hence, the present investigation was designed to unravel the unexplored facets of homeopathic medications such as Aconite, Arnica, Atropa, Conium, Ferrum phosphoricum.

Aconitum napellus contains an array of alkaloids which possess various pharmacological and toxicological properties. Arnica montana has long been used medicinally. It contains the toxin helenalin, which can be poisonous if large amounts of the plant are consumed. Contact with the plant can also cause skin irritation. The roots contain derivatives of thymol, which are used as fungicides and preservatives and may have some anti-inflammatory effect. When used topically in a gel, Arnica was found to have the same effect as the use of NSAIDs (ibuprofen) in treating the symptoms of hand osteoarthritis. A study found that the application of topical Arnica had no better effect than a placebo in the treatment of laser-induced bruising. Atropa belladonna is a branching herbaceous perennial, often growing as a subshrub, from a fleshy rootstock. Conium is a genus of two species of perennial herbaceous flowering plants in the family Apiaceae, native to Europe and the Mediterranean region (C. maculatum), and to southern Africa (C. chaerophylloides). By far the most familiar species is Conium maculatum (Hemlock or Poison Hemlock). When crushed, the leaves and root emit a rank, unpleasant odour sometimes compared to that of parsnips or mice. Iron(III) phosphate, also ferric orthophosphate, or ferric phosphate, $FePO_4$, is a phosphate of iron. It is one of the few molluscicides approved for use in the practice of organic farming. Unlike the older metaldehyde, it is non-toxic to pets and wildlife. It is also used rarely as an iron nutrition supplement and to reduce the risk of both hemorrhages and nosebleeds. This preparation is called called Ferrum phosphoricum. All homeopathic preparations are prepared by dilution and potentization.

Material and Methods

Drugs and reagents

Brewer's yeast was procured from local market. All the homeopathic medicines were commercially procured from K. R. Homeo Pharmacy, Pune. Paracetamol was kindly donated by Symed Pharmaceuticals, Hyderabad.

Animals

Wistar rats of both sexes, weighing 150 – 200 g were procured from National Toxicological Centre, Pune for the study. The animals were kept in polypropylene cages in a room maintained under controlled atmospheric conditions in animal house. The animals were fed with standard diet (Prashant Enterprises, Pune, India) and had free access to clean drinking water. The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) of Poona College of Pharmacy.

Experimental Design

The albino rats were randomly distributed in control and test groups of six animals each. They were fed with standard laboratory diet ad libitum and allowed free access to drinking water. The animals were kept in 12/12 hours dark – light cycle. One hour after starvation, the rectal temperature was recorded and animals having temperature between 37.00 and 37.50 C were selected for the study. Prior to the experiment, the rats were maintained in separate cages for 7 days and the animals with approximately constant rectal temperature were selected for the study. Pyrexia was induced by injecting subcutaneously 12% w/v suspension of Brewer's yeast in 0.9% NaCl (1ml/100gm. body weight) and allowed to feed[4]. Initial rectal temperature was recorded using a telethermometer by introducing 1 inch into the rectum and keeping it inside for 1 minute. The temperature first recorded after 18 hours of yeast administration was taken as zero hour reading. The animals in respective groups were administered with 0.4ml of drugs, vehicle and following homeopathic preparations:

DW: Distilled Water

Paracetamol: 150mg/kg p.o.

SDW: Sucussed Distilled Water 6c,12c, 30c, 200c,1M

DA: Dispensing Alcohol

SDA: Sucussed Dispensing Alcohol 6c, 12c, 30c, 200c,1M

AN: Aconite napellus 6c,12c, 30c, 200c, 1M

AN MT: Aconite napellus mother tincture

AM: Amica Montana 6c,12c, 30c, 200c, 1M

AM M: Amica Montana mother tincture

AB: Atropa belladona 6c,12c, 30c, 200c, 1M

AB MT: Atropa belladona mother tincture

CM: Conium maculatum 6c,12c, 30c, 200c, 1M

CM MT: Conium maculatum mother tincture

FP: Ferrum phosphoricum 6c, 12c, 30c, 200c, 1M

FP MT: Ferrum phosphoricum mother tincture

PG: Pyrogenum 6c, 12c, 30c, 200c, 1M

PG MT: Pyrogenum mother tincture

After the drugs were administered to the respective groups of rats, their body temperature was recorded at an interval of 1h, 2h, 3h and 4h and 24h. The mean temperature was found out for each group and compared with the value of paracetamol.

Statistical Analysis:

All data are presented as Mean±SEM and analyzed by one-way ANOVA, followed by Dunnett's test. p values <0.05 were considered statistically significant.

Fig 1 Effect of different dilutions and potencies of Aconite napellus on yeast induced pyrexia in laboratory rats.

Treatment	Rectal temperature (˚C)								
	1 day before	0 min	30 min	60 min	90 min	120 min	150 min	180 min	1 day later
Paracetamol	37.5±0.44	37.3±0.57	37.5±0.33***	38.4±0.53***	38.5±0.37***	38.4±0.41***	37.7±0.48	37.7±0.31	37.1±0.32
DW	37.4±0.62	37.6±0.55	39.6±0.61	39.8±0.63	40.7±0.63	39.4±0.33	39.5±0.54	38.3±0.47	37.1±0.49
SDW 6c	37.6±0.41	37.7±0.54	39.8±0.62	39.6±0.64	40.8±0.44	39.8±0.65	39.6±0.31	38.6±0.67	37.2±0.53
SDW 12c	37.1±0.42	37.5±0.41	39.7±0.65	39.7±0.57	40.9±0.33	39.3±0.39	39.6±0.33	38.1±0.52	37.3±0.54
SDW 30c	37.2±0.41	37.5±0.63	39.5±0.39	39.8±0.63	40.8±0.55	39.7±0.54	39.6±0.48	38.3±0.46	37.5±0.47
SDW 200c	37.3±0.51	37.5±0.43	39.6±0.60	39.9±0.37	40.8±0.32	39.8±0.71	39.4±0.67	38.7±0.58	37.6±0.58
SDW 1M	37.5±0.67	37.6±0.55	39.7±0.55	39.8±0.54	40.9±0.31	39.7±0.38	39.8±0.39	38.5±0.59	37.7±0.37
DA	37.4±0.47	37.9±0.38	39.6±0.56	39.7±0.58	40.8±0.46	39.6±0.23	39.7±0.45	38.3±0.49	37.5±0.46
SDA 6c	37.6±0.38	37.8±0.51	39.8±0.52	39.9±0.66	40.8±0.47	39.8±0.38	39.6±0.66	38.4±0.34	37.6±0.46
SDA 12c	37.5±0.37	37.7±0.48	39.7±0.48	39.9±0.64	40.8±0.51	39.8±0.48	39.8±0.37	38.3±0.67	37.7±0.53
SDA 30c	37.3±0.61	37.6±0.47	39.6±0.37	39.8±0.35	40.9±0.45	39.7±0.59	39.9±0.36	38.2±0.43	37.6±0.45
SDA 200c	37.4±0.43	37.6±0.63	39.9±0.63	39.7±0.28	40.9±0.56	39.6±0.48	39.9±0.57	38.9±0.48	37.7±0.57
SDA 1M	37.6±0.45	37.5±0.57	39.7±0.54	39.9±0.44	40.8±0.55	39.7±0.31	39.5±0.38	38.7±0.43	37.8±0.51
AN MT	37.5±0.57	37.3±0.54	39.8±0.63	39.7±0.46	40.9±0.54	39.8±0.57	39.7±0.46	38.9±0.56	37.9±0.53
AN 6c	37.3±0.37	37.5±0.56	39.7±0.63	39.6±0.42	40.7±0.51	39.9±0.48	39.7±0.53	38.8±0.57	37.7±0.67
AN 12c	37.6±0.43	37.3±0.43	39.8±0.67	39.8±0.48	40.7±0.57	39.7±0.59	39.6±0.47	38.7±0.66	37.6±0.46
AN 30c	37.5±0.32\	37.5±0.66	39.8±0.69	39.7±0.66	40.8±0.55	39.6±0.53	39.6±0.59	38.3±0.55	37.5±0.52
AN 90c	37.3±0.63	37.4±0.62	39.7±0.19	39.2±0.52	40.8±0.36	39.5±0.49	39.8±0.51	38.6±0.64	37.6±0.53
AN 1M	37.2±0.65	37.2±0.46	39.8±0.64	39.4±0.47	40.7±0.39	39.6±0.38	39.7±0.49	38.3±0.63	37.7±0.49

Values are expressed as mean ± SEM (n=6) *P<0.05 **P<0.01 ***P<0.001 when compared to controlDW : Distilled Water, SDW : Sucussed Distilled Water, DA : Dispensing Alcohol, SDA : Sucussed Dispensing Alcohol, AN : Aconite napellus, AN MT: Aconite napellus mother tincture

Fig 2 Effect of different dilutions and potencies of Amica Montana on yeast induced pyrexia in laboratory rats.

Treatment	Rectal temperature (˚C)								
	1 day before	0 min	30 min	60 min	90 min	120 min	150 min	180 min	1 day later
Paracetamol	37.3±0.26	37.3±0.37	37.6±0.54***	38.5±0.34***	38.2±0.43***	38.2±0.55***	37.3±0.47	37.5±0.33	37.5±0.26
DW	37.5±0.67	37.6±0.47	39.4±0.60	39.9±0.42	40.4±0.54	39.4±0.32	39.6±0.33	38.7±0.43	37.3±0.42
SDW 6c	37.6±0.54	37.4±0.55	39.2±0.50	39.8±0.41	40.3±0.48	39.6±0.43	39.8±0.42	38.4±0.62	37.6±0.44
SDW 12c	37.3±0.46	37.6±0.42	39.1±0.64	39.8±0.31	40.5±0.39	39.5±0.47	39.7±0.49	38.4±0.59	37.5±0.46
SDW 30c	37.6±0.67	37.6±0.68	39.2±0.39	39.9±0.46	40.6±0.51	39.6±0.53	39.6±0.56	38.6±0.48	37.4±0.36
SDW 200c	37.3±0.54	37.7±0.46	39.7±0.60	39.8±0.63	40.8±0.38	39.7±0.54	39.6±0.51	38.5±0.51	37.6±0.41
SDW 1M	37.5±0.66	37.6±0.52	39.2±0.51	39.7±0.56	40.9±0.32	39.8±0.42	39.3±0.48	38.6±0.52	37.5±0.44
DA	37.6±0.46	37.5±0.34	39.3±0.56	39.8±0.37	40.8±0.48	39.9±0.53	39.4±0.53	38.5±0.43	37.3±0.33
SDA 6c	37.6±0.27	37.8±0.57	39.6±0.52	39.8±0.44	40.9±0.45	39.7±0.45	39.5±0.55	38.6±0.34	37.4±0.31
SDA 12c	37.5±0.33	37.7±0.48	39.8±0.46	39.9±0.37	40.7±0.52	39.7±0.56	39.6±0.48	38.8±0.65	37.6±0.41
SDA 30c	37.3±0.26	37.6±0.45	39.6±0.31	39.7±0.53	40.8±0.43	39.8±0.47	39.6±0.54	38.7±0.42	37.5±0.42
SDA 200c	37.4±0.46	37.5±0.61	39.5±0.62	39.8±0.32	40.9±0.54	39.7±0.41	39.8±0.44	38.7±0.41	37.2±0.41
SDA 1M	37.5±0.43	37.3±0.51	39.7±0.51	39.8±0.53	40.8±0.59	39.7±0.52	39.5±0.54	38.5±0.42	37.6±0.57
AM MT	37.7±0.56	37.7±0.58	39.8±0.61	39.6±0.65	40.7±0.51	39.8±0.52	39.3±0.55	38.7±0.51	37.3±0.38
AM 6c	37.2±0.37	37.6±0.55	39.8±0.62	39.5±0.23	40.8±0.59	39.8±0.52	39.6±0.43	38.6±0.52	37.6±0.51
AM 12c	37.3±0.48	37.5±0.44	39.7±0.72	39.7±0.36	40.7±0.54	39.7±0.43	39.6±0.58	38.6±0.55	37.4±0.11
AM 30c	37.5±0.39	37.6±0.62	39.8±0.63	39.6±0.12	40.7±0.59	39.8±0.63	39.5±0.45	38.5±0.41	37.5±0.33
AM 90c	37.3±0.51	37.6±0.61	39.9±0.13	39.7±0.54	40.8±0.39	39.7±0.59	39.6±0.32	38.5±0.51	37.6±0.45
AM 1M	37.3±0.62	37.4±0.46	39.9±0.65	39.3±0.35	40.4±0.38	39.6±0.48	39.5±0.31	38.3±0.51	37.4±0.37

Values are expressed as mean ± SEM (n=6) *P<0.05 **P<0.01 ***P<0.001 when compared to control DW : Distilled Water, SDW : Sucussed Distilled Water, DA : Dispensing Alcohol, SDA : Sucussed Dispensing Alcohol, AM : Amica montana, AM MT: Amica Montana mother tincture

Fig 3 Effect of different dilutions and potencies of Atropa belladona on yeast induced pyrexia in laboratory rats.

Treatment	Rectal temperature (˚C)								
	1 day before	0 min	30 min	60 min	90 min	120 min	150 min	180 min	1 day later
Paracetamol	37.1±0.23	37.2±0.32	37.9±0.56***	38.5±0.45***	38.7±0.43***	38.5±0.54***	37.8±0.57	37.4±0.33	37.4±0.36
DW	37.4±0.63	37.3±0.45	39.4±0.64	39.9±0.34	40.6±0.54	39.8±0.38	39.6±0.43	38.6±0.43	37.2±0.52
SDW 6c	37.5±0.53	37.6±0.52	39.8±0.56	39.8±0.62	40.9±0.48	39.9±0.45	39.7±0.32	38.3±0.62	37.5±0.54
SDW 12c	37.2±0.45	37.4±0.43	39.6±0.64	39.8±0.56	40.8±0.39	39.8±0.49	39.6±0.39	38.5±0.59	37.3±0.56
SDW 30c	37.3±0.65	37.6±0.67	39.3±0.35	39.9±0.69	40.7±0.51	39.8±0.54	39.7±0.46	38.4±0.48	37.6±0.46
SDW 200c	37.4±0.58	37.6±0.45	39.7±0.61	39.8±0.39	40.9±0.38	39.7±0.51	39.5±0.61	38.7±0.51	37.5±0.51
SDW 1M	37.3±0.61	37.4±0.56	39.8±0.56	39.7±0.56	40.8±0.32	39.8±0.48	39.3±0.38	38.5±0.52	37.3±0.34
DA	37.4±0.43	37.5±0.34	39.6±0.53	39.8±0.54	40.9±0.48	39.5±0.53	39.4±0.43	38.7±0.43	37.2±0.43
SDA 6c	37.7±0.29	37.6±0.54	39.7±0.59	39.8±0.67	40.7±0.45	39.8±0.48	39.3±0.65	38.6±0.34	37.4±0.41
SDA 12c	37.5±0.32	37.6±0.45	39.6±0.47	39.9±0.65	40.7±0.52	39.7±0.58	39.6±0.38	38.4±0.65	37.5±0.51
SDA 30c	37.2±0.75	37.1±0.47	39.5±0.36	39.7±0.34	40.9±0.43	39.6±0.49	39.5±0.34	38.5±0.42	37.4±0.42
SDA 200c	37.5±0.49	37.3±0.65	39.8±0.67	39.8±0.21	40.7±0.54	39.5±0.48	39.7±0.54	38.8±0.41	37.3±0.51
SDA 1M	37.1±0.43	37.2±0.59	39.6±0.56	39.8±0.43	40.7±0.59	39.6±0.51	39.4±0.34	38.6±0.42	37.6±0.57
AB MT	37.6±0.54	37.4±0.51	39.7±0.65	39.6±0.49	40.9±0.51	39.8±0.57	39.2±0.45	38.7±0.51	37.5±0.58
AB 6c	37.3±0.32	37.5±0.58	39.6±0.64	39.5±0.43	40.6±0.59	39.7±0.58	39.5±0.53	38.4±0.52	37.6±0.61
AB 12c	37.5±0.43	37.4±0.49	39.7±0.74	39.7±0.49	40.6±0.54	39.6±0.49	39.4±0.48	38.7±0.65	37.6±0.41
AB 30c	37.4±0.34	37.6±0.63	39.9±0.67	39.6±0.67	40.5±0.59	39.5±0.53	39.6±0.55	38.6±0.51	37.4±0.53
AB 200c	37.1±0.59	37.5±0.64	39.8±0.17	39.7±0.51	40.5±0.39	39.4±0.49	39.7±0.52	38.6±0.61	37.6±0.55
AB 1M	37.4±0.61	37.3±0.47	39.7±0.67	39.6±0.45	40.3±0.38	39.5±0.38	39.5±0.41	38.4±0.61	37.5±0.47

Values are expressed as mean ± SEM (n=6) *P<0.05 **P<0.01 ***P<0.001 when compared to control DW : Distilled Water, SDW : Sucussed Distilled Water, DA : Dispensing Alcohol, SDA : Sucussed Dispensing Alcohol, AB : Atropa belladona , AB MT: Atropa belladona mother tincture

Fig 4 Effect of different dilutions and potencies of Conium maculatum on yeast induced pyrexia in laboratory rats.

Treatment	Rectal temperature (˚C)								
	1 day before	0 min	30 min	60 min	90 min	120 min	150 min	180 min	1 day later
Paracetamol	37.2±0.22	37.2±0.32	37.9±0.16***	38.5±0.42***	38.7±0.43***	38.4±0.52***	37.8±0.34	37.3±0.32	37.4±0.26
DW	37.4±0.61	37.3±0.45	39.4±0.34	39.9±0.32	40.6±0.54	39.5±0.32	39.6±0.43	38.2±0.42	37.2±0.22
SDW 6c	37.6±0.52	37.6±0.52	39.8±0.56	39.8±0.61	40.9±0.48	39.5±0.43	39.7±0.31	38.3±0.63	37.5±0.24
SDW 12c	37.4±0.42	37.4±0.43	39.6±0.24	39.8±0.52	40.8±0.39	39.4±0.44	39.6±0.31	38.2±0.54	37.3±0.26
SDW 30c	37.3±0.62	37.6±0.67	39.3±0.55	39.9±0.61	40.7±0.51	39.6±0.51	39.7±0.42	38.3±0.42	37.6±0.36
SDW 200c	37.2±0.53	37.6±0.45	39.7±0.41	39.8±0.32	40.9±0.38	39.3±0.50	39.5±0.62	38.3±0.53	37.5±0.41
SDW 1M	37.5±0.31	37.4±0.56	39.8±0.36	39.7±0.53	40.8±0.32	39.5±0.42	39.3±0.33	38.5±0.52	37.3±0.54
DA	37.6±0.43	37.5±0.34	39.6±0.43	39.8±0.52	40.9±0.48	39.3±0.51	39.4±0.42	38.4±0.41	37.2±0.33
SDA 6c	37.4±0.39	37.6±0.54	39.7±0.49	39.8±0.62	40.7±0.45	39.5±0.41	39.3±0.61	38.5±0.32	37.4±0.21
SDA 12c	37.5±0.2	37.6±0.45	39.6±0.47	39.9±0.61	40.7±0.52	39.3±0.52	39.6±0.31	38.5±0.62	37.5±0.31
SDA 30c	37.3±0.75	37.1±0.47	39.5±0.26	39.7±0.33	40.9±0.43	39.2±0.43	39.5±0.33	38.6±0.43	37.4±0.52
SDA 200c	37.2±0.49	37.3±0.65	39.8±0.57	39.8±0.21	40.7±0.54	39.3±0.41	39.7±0.51	38.5±0.42	37.3±0.41
SDA 1M	37.4±0.43	37.2±0.59	39.6±0.36	39.8±0.43	40.7±0.59	39.2±0.52	39.4±0.33	38.4±0.41	37.6±0.37
CM MT	37.5±0.54	37.4±0.53	39.7±0.55	39.6±0.44	40.9±0.51	39.4±0.53	39.2±0.42	38.5±0.54	37.5±0.28
CM 6c	37.4±0.32	37.5±0.56	39.6±0.44	39.5±0.45	40.6±0.59	39.4±0.54	39.5±0.52	38.4±0.54	37.6±0.61
CM 12c	37.5±0.43	37.4±0.42	39.7±0.54	39.7±0.43	40.6±0.54	39.5±0.44	39.4±0.43	38.5±0.63	37.6±0.21
CM 30c	37.4±0.34	37.6±0.62	39.1±0.37	39.1±0.57*	39.7±0.59*	39.4±0.52	38.2±0.54	38.1±0.53	37.4±0.33
CM 200c	37.6±0.59	37.6±0.61	39.1±0.27**	39.1±0.54**	38.5±0.39**	38.7±0.42**	38.2±0.53	37.9±0.62	37.6±0.45
CM 1M	37.3±0.61	37.1±0.46	38.1±0.27***	38.8±0.42***	38.3±0.38***	38.5±0.33***	38.1±0.41	37.4±0.61	37.5±0.27

Values are expressed as mean ± SEM (n=6) *P<0.05 **P<0.01 ***P<0.001 when compared to control DW : Distilled Water, SDW : Sucussed Distilled Water, DA :Dispensing Alcohol, SDA : Sucussed Dispensing Alcohol, CM : Conium maculatum, CM MT: Conium maculatum mother tincture

Fig 5 Effect of different dilutions and potencies of Ferrum phosphoricum on yeast induced pyrexia in laboratory rats.

Treatment	Rectal temperature (˚C)								
	1 day before	0 min	30 min	60 min	90 min	120 min	150 min	180 min	1 day later
Paracetamol	37.1±0.23	37.2±0.32	37.9±0.56***	38.5±0.45***	38.7±0.43***	38.5±0.54***	37.8±0.57	37.4±0.33	37.4±0.36
DW	37.4±0.63	37.3±0.45	39.4±0.64	39.9±0.34	40.6±0.54	39.8±0.38	39.6±0.43	38.6±0.43	37.2±0.52
SDW 6c	37.5±0.53	37.6±0.52	39.8±0.56	39.8±0.62	40.9±0.48	39.9±0.45	39.7±0.32	38.3±0.62	37.5±0.54
SDW 12c	37.2±0.45	37.4±0.43	39.6±0.64	39.8±0.56	40.8±0.39	39.8±0.49	39.6±0.39	38.5±0.59	37.3±0.56
SDW 30c	37.3±0.65	37.6±0.67	39.3±0.35	39.9±0.69	40.7±0.51	39.8±0.54	39.7±0.46	38.4±0.48	37.6±0.46
SDW 200c	37.4±0.58	37.6±0.45	39.7±0.61	39.8±0.39	40.9±0.38	39.7±0.51	39.5±0.61	38.7±0.51	37.5±0.51
SDW 1M	37.3±0.61	37.4±0.56	39.8±0.56	39.7±0.56	40.8±0.32	39.8±0.48	39.3±0.38	38.5±0.52	37.3±0.34
DA	37.4±0.43	37.5±0.34	39.6±0.53	39.8±0.54	40.9±0.48	39.5±0.53	39.4±0.43	38.7±0.43	37.2±0.43
SDA 6c	37.7±0.29	37.6±0.54	39.7±0.59	39.8±0.67	40.7±0.45	39.8±0.48	39.3±0.65	38.6±0.34	37.4±0.41
SDA 12c	37.5±0.32	37.6±0.45	39.6±0.47	39.9±0.65	40.7±0.52	39.7±0.58	39.6±0.38	38.4±0.65	37.5±0.51
SDA 30c	37.2±0.75	37.1±0.47	39.5±0.36	39.7±0.34	40.9±0.43	39.6±0.49	39.5±0.34	38.5±0.42	37.4±0.42
SDA 200c	37.5±0.49	37.3±0.65	39.8±0.67	39.8±0.21	40.7±0.54	39.5±0.48	39.7±0.54	38.8±0.41	37.3±0.51
SDA 1M	37.1±0.43	37.2±0.59	39.6±0.56	39.8±0.43	40.7±0.59	39.6±0.51	39.4±0.34	38.6±0.42	37.6±0.57
FP MT	37.6±0.54	37.4±0.51	39.7±0.65	39.6±0.49	40.9±0.51	39.8±0.57	39.2±0.45	38.7±0.51	37.5±0.58
FP 6c	37.3±0.32	37.5±0.58	39.6±0.64	39.5±0.43	40.6±0.59	39.7±0.58	39.5±0.53	38.4±0.52	37.6±0.61
FP 12c	37.5±0.43	37.4±0.49	39.7±0.74	39.7±0.49	40.6±0.54	39.6±0.49	39.4±0.48	38.7±0.65	37.6±0.41
FP 30c	37.4±0.34	37.6±0.63	39.9±0.67	39.6±0.67	40.5±0.59	39.5±0.53	39.6±0.55	38.6±0.51	37.4±0.53
FP 200c	37.1±0.59	37.5±0.64	39.8±0.17	39.7±0.51	40.5±0.39	39.4±0.49	39.7±0.52	38.6±0.61	37.6±0.55
FP 1M	37.4±0.61	37.3±0.47	39.7±0.67	39.6±0.45	40.3±0.38	39.5±0.38	39.5±0.41	38.4±0.61	37.5±0.47

Values are expressed as mean ± SEM (n=6) *P<0.05 **P<0.01 ***P<0.001 when compared to control DW : Distilled Water, SDW : Sucussed Distilled Water, DA : Dispensing Alcohol, SDA : Sucussed Dispensing Alcohol, FP : Ferrum phosphoricum, FP MT: Ferrum phosphoricum mother tincture

Fig 6 Effect of different dilutions and potencies of Pyrogenium on yeast induced pyrexia in laboratory rats.

Treatment	Rectal temperature (˚C)								
	1 day before	0 min	30 min	60 min	90 min	120 min	150 min	180 min	1 day later
Paracetamol	37.3±0.28	37.1±0.31	37.8±0.53***	38.4±0.22***	38.4±0.42***	38.6±0.53***	37.4±0.37	37.1±0.31	37.3±0.33
DW	37.4±0.66	37.5±0.43	39.6±0.63	39.2±0.43	40.3±0.51	39.7±0.31	39.5±0.23	38.2±0.41	37.2±0.57
SDW 6c	37.6±0.54	37.4±0.51	39.8±0.54	39.3±0.52	40.5±0.42	39.8±0.42	39.4±0.42	38.5±0.62	37.1±0.52
SDW 12c	37.5±0.41	37.6±0.42	39.6±0.61	39.6±0.56	40.3±0.34	39.5±0.43	39.6±0.59	38.3±0.52	37.4±0.55
SDW 30c	37.5±0.62	37.7±0.63	39.8±0.33	39.6±0.39	40.2±0.53	39.4±0.54	39.6±0.36	38.4±0.41	37.5±0.42
SDW 200c	37.4±0.52	37.8±0.42	39.6±0.62	39.7±0.24	40.1±0.32	39.5±0.52	39.1±0.61	38.5±0.53	37.3±0.51
SDW 1M	37.6±0.64	37.5±0.51	39.5±0.55	39.4±0.56	40.6±0.31	39.4±0.43	39.2±0.48	38.6±0.54	37.4±0.44
DA	37.4±0.44	37.7±0.32	39.7±0.51	39.3±0.53	40.2±0.44	39.3±0.52	39.4±0.53	38.7±0.45	37.5±0.33
SDA 6c	37.5±0.23	37.4±0.52	39.6±0.55	39.2±0.62	40.5±0.42	39.9±0.41	39.6±0.45	38.5±0.33	37.5±0.31
SDA 12c	37.6±0.31	37.2±0.41	39.8±0.42	39.8±0.25	40.6±0.51	39.8±0.55	39.5±0.38	38.3±0.62	37.6±0.51
SDA 30c	37.6±0.61	37.7±0.42	39.5±0.33	39.8±0.54	40.7±0.45	39.7±0.42	39.3±0.44	38.2±0.41	37.4±0.42
SDA 200c	37.5±0.44	37.2±0.61	39.3±0.63	39.7±0.31	40.8±0.56	39.6±0.43	39.5±0.24	38.1±0.46	37.4±0.31
SDA 1M	37.3±0.44	37.1±0.51	39.5±0.51	39.8±0.13	40.9±0.53	39.2±0.50	39.4±0.34	38.5±0.42	37.3±0.27
PG MT	37.4±0.53	37.2±0.50	39.2±0.62	39.7±0.49	40.5±0.52	39.2±0.51	39.3±0.55	38.3±0.53	37.5±0.58
PG 6c	37.6±0.32	37.6±0.52	39.5±0.61	39.8±0.33	40.6±0.51	39.1±0.52	39.5±0.13	38.2±0.52	37.6±0.41
PG 12c	37.3±0.41	37.4±0.40	39.6±0.61	39.7±0.29	40.7±0.51	39.4±0.45	39.2±0.38	38.1±0.65	37.7±0.31
PG 30c	37.4±0.31	37.2±0.60	39.6±0.60	39.6±0.27	40.8±0.54	39.6±0.53	39.4±0.25	38.2±0.53	37.4±0.13
PG 200c	37.2±0.51	37.4±0.62	39.7±0.19	39.7±0.31	40.9±0.32	39.6±0.45	39.4±0.22	38.3±0.25	37.5±0.25
PG 1M	37.5±0.62	37.3±0.43	39.7±0.63	39.2±0.35	40.7±0.32	39.7±0.30	39.4±0.31	38.2±0.60	37.2±0.37

Values are expressed as mean ± SEM (n=6) *P<0.05 **P<0.01 ***P<0.001 when compared to control DW : Distilled Water, SDW : Sucussed Distilled Water, DA : Dispensing Alcohol, SDA : Sucussed Dispensing Alcohol, PG : Pyrogenium, PG MT: Pyrogenium mother tincture

Results

In all the experimental rats, the initial rectal temperature was found to be equal to 37.5^0C. After a period of 18 hours, the mean rectal temperature showed a continuous rise in all the groups of animals. The rectal temperature was continuously monitored at 0, 30, 60, 90, 120,150,180 minutes and 24 hours after the administration of drugs using a telethermometer. The rectal temperature showed a continuous rise in all the groups of animals and peaked at the 90^{th} minute and then decreased till 180^{th} minute. After 24 hours of the drug treatment, the rectal temperature was found to be equal to the mean temperature of 37.5^0C. In the group of animals treated with Conium at the doses of 30c, 200c, and 1M there was significant inhibition of rise in rectal temperature. At a dose of 30c conium was able to inhibit the rise in rectal temperature at 60 and 90 minutes ($p<0.05$). At a dose of 200c conium was able to inhibit the elevation of rectal temperature at 30, 60, 90 and 120 minutes.($p<0.01$). At a dose of 1M conium was able to inhibit the elevation of rectal temperature at 30, 60, 90 and 120 minutes ($p<0.001$)(figure 4).The rectal temperature in all the animals treated with Aconite, Arnica, Belladona, and Pyrogenium did not show any fall with respect to time when compared with the vehicle treated group of animals.(figure 1 to 4 and 5).

Discussion

Pyrexia is characterized by an uncontrolled increase in body temperature that exceeds the body's ability to dissipate heat. Exogenous heat exposure and endogenous heat production are two mechanisms by which hyperthermia can lead to abnormally elevated internal temperatures that may be lethal. Excessive heat production can easily cause hyperthermia despite physiologic and behavioral control of body temperature[1,2]. The term pyrogen is used to describe any substance that leads to fever. Exogenous pyrogens are mostly microbial products, microbial toxins, or whole microorganisms. The classic example of an exogenous pyrogen is the lipopolysaccharide endotoxin produced by all gram-negative bacteria. The synthesis and release of endogenous pyrogenic cytokines are induced by exogenous pyrogens which are derived from bacterial or fungal sources. Yeast is a fungus that leads to elevation of prostaglandins which are responsible for fever. During fever, levels of prostaglandin E_2 (PGE_2) are increased in hypothalamic tissue and the third cerebral ventricle. The concentrations of PGE_2 are highest near the circumventricular vascular organs (organum vasculosum of lamina terminalis)—networks of enlarged capillaries surrounding the hypothalamic regulatory centers. The synthesis of PGE_2 depends on the constitutively expressed enzyme cyclooxygenase. Arachidonic acid which is the substrate for cyclooxygenase enzyme is released from the cell membrane which in turn is the rate-limiting step in the synthesis of PGE_2. Inhibitors of cyclooxygenase are potent antipyretics. The antipyretic potential of various drugs could be directly correlated to the suppression cyclooxygenase in the brain. Acetaminophen is a poor cyclooxygenase inhibitor in peripheral tissue and is without noteworthy anti-inflammatory activity; in the brain, however, acetaminophen is oxidized by the p450 cytochrome system, and the oxidized form is responsible for inhibition of cyclooxygenase activity[5]. Moreover, in the brain, the inhibition of another enzyme, COX-3, by acetaminophen may be responsible for its antipyretic effect.

Belladonna has been used in traditional treatments for centuries for an assortment of conditions including headache, menstrual symptoms, peptic ulcer disease, histaminic reaction, inflammation, and motion sickness, with at least one 19th century eclectic medicine journal explaining how to prepare a Belladonna tincture for direct administration to patients. Homeopathic belladonna preparations have been sold as treatments for various conditions, although there is no scientific evidence to support their efficacy[6,7]. Clinically and in research trials, the most common preparation is diluted to the 30C level in homeopathic notation. This level of dilution does not contain any of the original plant, although preparations with lesser dilutions which statistically contain trace amounts of the plant are advertised for sale[8].The central nervous system effects of atropine include memory disruption, which may lead to severe confusion[9]. Aconites have been used more recently in murder plots; they contain the Chemical alkaloids aconitine, mesaconitine, hypaconitine and jesaconitine, which are highly toxic[10]. Arnica contains helenalin, which can be poisonous if large amounts of the plant are eaten. Contact with the plant can also cause skin irritation. The roots contain derivatives of thymol, which are used as fungicides and preservatives and may have some anti-inflammatory effect[11]. When used topically in a gel, Arnica was found to have the same effect as the use of NSAIDs (ibuprofen) in treating the symptoms of hand osteoarthritis[12]. A study found that the application of topical Arnica had no better effect than a placebo in the treatment of laser-induced bruising. Ferrum phos is prescribed to treat a plethora of diseases in biochemic medication.

Conium contains the piperidine alkaloids coniine, N-methylconiine, conhydrine, pseudoconhydrine and γ-coniceine (or g-coniceïne), which is the precursor of the other hemlock alkaloids[13].The most important and toxic of these is coniine, which has a chemical structure similar to nicotine. Coniine is a neurotoxin, which disrupts the workings of the central nervous system and is toxic to humans and all classes of livestock. Ingestion in any quantity can result in respiratory collapse and death. Coniine causes death by blocking the neuromuscular junction in a manner similar to curare; this results in an ascending muscular paralysis with eventual paralysis of the respiratory muscles which results in death due to lack of oxygen to the heart and brain. Coniine, γ-coniceine and N-methylconiine, the conhydrine and ψ-conhydrine are the various phytochemicals present in Conium. C. maculatum is poisonous to animals. In a short time the alkaloids produce a potentially fatal neuromuscular blockage when the respiratory muscles are affected. Acute toxicity, if not lethal, may resolve in the spontaneous recovery of the affected animals provided further exposure is avoided. It has been observed that poisoned animals tend to return to feed on this plant. It has been used as a sedative and for its antispasmodic properties. It was also used by Greek and Persian physicians for a variety of problems, such as arthritis. It wasn't always effective, however, as the difference between a therapeutic and a toxic amount (the therapeutic index) is very slight. Overdoses can produce paralysis and loss of speech, followed by depression of the respiratory function, and then death[14,15]. In the present investigation the conium demonstrated a dose dependent anti pyretic effect in the laboratory animals. It is well known that yeast least to pyrexia due to production of prostaglandins which reset the temperature regulation centre at the hypothalamus. It could be deduced that conium when diluted and potentized according to the norms laid down in the homeopathic system of medicine possesses ability to reverse the elevated rectal temperature. Homeopathy works due to molecular transformations elicited in various biological systems such as microorganisms and plants[16,17].

However, the specific mechanism underlying the pharmacological effect needs to be unraveled by measuring the levels of various pyrogens and circulating prostaglandins. This provides ample and obvious opportunities to pursue preclinical retrospective research.

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