OPEN ACCESS

ORIGINAL ARTICLE

Evaluation of Antipyretic Effects of Ultrahigh Dilutions of *Baptisia tinctoria* in Comparison with Paracetamol

Tayyeba Rehman[1,*], Saeed Ahmad[2], Waheed Mumtaz Abbasi[3], Aymen Owais Ghauri[4], Khalid Akhtar[1], Muhammad Bilal[5], Shifa Shafique[1], Muhammad Adeel Arshad[2]

[1]*University College of Conventional Medicine, Faculty of Pharmacy and Alternative Medicine, The Islamia University of Bahawalpur, Bahawalpur, Pakistan*

[2]*Department of Pharmacy, Faculty of Pharmacy and Alternative Medicine, The Islamia University of Bahawalpur, Bahawalpur, Pakistan*

[3]*Medical and Health Division, The Islamia University of Bahawalpur, Bahawalpur, Pakistan*

[4]*Department of Eastern Medicine, Jinnah University for Women, Karachi, Pakistan*

[5]*First Department of Internal Medicine, University of Toyama, Toyama, Japan*

Authors' Contributions

1 Conception & Study Design, Data Collection, Data Analysis, Drafting, Critical Review.
2 Conception & Study Design, Data Analysis, Critical Review.
3,5,6 Data Analysis, Drafting, Critical Review.
4 Data Collection, Drafting, Critical Review.
7,8 Data Collection, Data Analysis, Drafting.

Article info.
Received: November 22, 2018
Accepted: July 11, 2019

Funding Source: *Nil*
Conflict of Interest: *Nil*

Cite this article: *Rehman T, Ahmad S, Abbasi WM, Ghauri AO, Akhtar K, Bilal M, Shafique S, Arshad MA. Evaluation of Antipyretic Effects of Ultrahigh Dilutions of Baptisia tinctoria in Comparison with Paracetamol. RADS J. Pharm. Pharm. Sci. 2019; 7(2): 68-72.*

Address of Correspondence Author:
tayeba.rehman@yahoo.com

ABSTRACT

Introduction: Homeopathy being an alternative treatment option has many controversies. The study aims to estimate the antipyretic effects of *Baptisia tinctoria* (200c and 1M ultrahigh dilutions) in animal fever model.

Methods: This study used *Saccharomyces cerevisiae* induced fever model. Animals were divided into 4 groups namely, negative control, positive control and *Baptisia tinctoria* 200c and 1M groups. During study, after each hour rectal temperature was checked. Paracetamol and homeopathic *Baptisia tinctoria* (200c and 1M) and paracetamol were given orally. One way statistical analysis was done with ANOVA followed by post hoc test. Significance level was $p \leq 0.05$.

Results: *B. tinctoria* in both potencies significantly reduced fever in rabbits compared to negative control group ($p \leq 0.05$). At the end of study, paracetamol reduced by 2.5°F, while *B. tinctoria* 200c reduced by 1.7°F temperature and *B. tinctoria* 1M reduced by 1.9°F.

Conclusion: The study revealed that *B. tinctoria* showed its activity against fever, however, it has weaker action as compared to paracetamol.

Keywords: Antipyretic, *Baptisia tinctoria*, homeopathy, ultrahigh dilutions.

INTRODUCTION

Hyperpyrexia (fever) is an adaptive reaction to various inflammatory and infectious problems [1]. It can cause damage to the brain [2]. Several medicines in homeopathy are being traditionally used for fever. Some of the effective antipyretics include *Aconitum napellus* [3], *Nux vomica* [4], *Typhoidinum* [5] *Belladonna* and *Pyrogenium* [6].

Homeopathy works on the principle of similarity that the medicine having similarity to disease picture could treat the disease [7]. *Baptisia* is a remedy for septic states especially septicemia that comes on rapidly, have low-grade fever type and have a short duration of action [8]. *S. cerevisiae* induced pyrexia model was used to induce fever. *S. cerevisiae* causes elevation in temperature by elevating plasma levels of inflammatory cytokines [9-11]. Several studies in literature used *S. cerevisiae* induced pyrexia model [9, 11-16].

Literature search showed that no study was done to evaluate antipyretic effects of homeopathic medicine

Baptisia tinctoria. The current investigation was done primarily to examine if *Baptisia tinctoria* ultrahigh dilutions could show antipyretic activity in *S. cerevisiae* induced pyrexia model.

MATERIALS AND METHODS

Materials

Paracetamol GlaxoSmithKline, Pakistan, Limited, *Baptisia tinctoria* 200c (Lot No. 9161211), *Baptisia tinctoria* 1M (Lot No. 7020207), *Saccharomyces cerevisiae*, normal saline, distilled water, digital thermometer were used.

System Performance Controls

Paracetamol was used as positive control of the experiment and administered to one group contained 6 rabbits. It was administered orally at the dosage of 150 mg/kg body weight. Alcohol (5 drops of medicine in purified water) was used as negative control and given orally to one group contained 6 rabbits.

Quality Control

For experiment conduction, 3 persons were trained for animal handling. Animals were carefully and gently held and treated during temperature measurement to minimize stress-induced hyperthermia. Only skilled persons were allowed to handle and measure the temperature of rabbits.

Animals

Adult healthy rabbits of local strain were purchased from the market. The weight of rabbits ranged from 1000 to 1700 grams, and both male and female rabbits were included in the study. All the animals stayed in the air-conditioned animal house situated in Railway Campus, The Islamia University Bahawalpur. Standard diet and water were provided *ad libitum*. Acclimatization for 7 days prior to study was carried out.

Ethics Approval

The study was approved by Pharmacy Research Ethics Committee (PREK), The Islamia University of Bahawalpur, Pakistan (88-2015/PREC).

Experimental Setup

Rabbits were divided in four groups each having animals. The activity was performed according to methodology of Ahamd *et al*. [5]. >1°F increase in temperature of rabbits was inclusion criteria. Group 1 and 2 were control groups namely negative control (Alcohol) and positive control (Paracetamol). Group 3 and 4 were experimental groups and received *B. tinctoria* 1M and 200c, respectively.

Intervention

Paracetamol was administered orally at the dosage of 150 mg/kg [13] after 4 h of yeast injection. *B. tinctoria* 1M and 200c were given through oral route after mixing in purified water (5cc). All homeopathic medicines were given after 4 hours of yeast injection.

Statistical Methods

Results and data obtained by this study were evaluated using SPSS (I.B.M.SPSS. statistics.v20_32bit_oxava.com). ANOVA followed by post hoc test was used for checking any statistical significance. P <0.05 was taken as significant.

RESULTS

Table **1** described the baseline characteristics of different groups. At the 4th hour after yeast administration temperature of more than 1°F was raised in all the rabbits.

Table 1. Body weight and temperature of different groups (baseline readings).

Characteristics	Negative Control	Paracetamol	*B. tinctoria* 200C	*B. tinctoria* 1M
Body weight (kg)	102.6 ± 0.31	1.3 ± 0.07	1.3 ± 0.09	1.3 ± 0.08
Temperature (°F)	102.6 ± 0.31	102.2 ± 0.86	102.6 ± 0.22	102.7 ± 0.25

Table **2** showed the temperature variation of negative control group was continuously increased till the 8th hour of study from 102.6 to 104.9. Afterwards slight decrease in temperature was observed. Paracetamol, positive control of study, decreased the temperature markedly during first hour of study. However, a slight increase of temperature was seen that was going to normal temperature in the 10th hour of the experiment. *B. tinctoria* 1M group showed an increase of 1.9°F temperature after 4th hour of administration of baker's yeast. Medicine showed a gradual decrease of temperature from 104.6°F to 104.1°F in first hour (p value 0.203), at 2nd hour of medicine administration to 103.9°F (p value 0.06), at 3rd hour to 102.9°F (p value <0.001), at 4th hour to 102.7°F (p value <0.001), at 5th hour to 102.8°F (p value 0.001) and again showed decrease of temperature to 102.7°F (p value 0.041) in 6th hour of medicine administration. "*B. tinctoria* 200c" group showed an increase of temperature from 102.6 ± 0.22°F to 104.3±.26°F after 4 hour of yeast administration. After 1 hour of *B. tinctoria* 200c administration, temperature decreased to 103.8 ± 0.47°F (p value 0.08), at 2nd hour temperature decreased to 103.7 ± 0.17°F (p value 0.01), at 3rd hour temperature decreased to 103 ± 0.31°F (p value <0.001), at 4th hour temperature decreased to 102.4±.56°F (p value <0.001), at 5th hour temperature decreased to 103±.25°F (p value 0.004), at 6th hour temperature decreased towards normal baseline temperature (p value 0.021). Figure **1** compares antipyretic effects of both potencies of *B. tinctoria* with paracetamol.

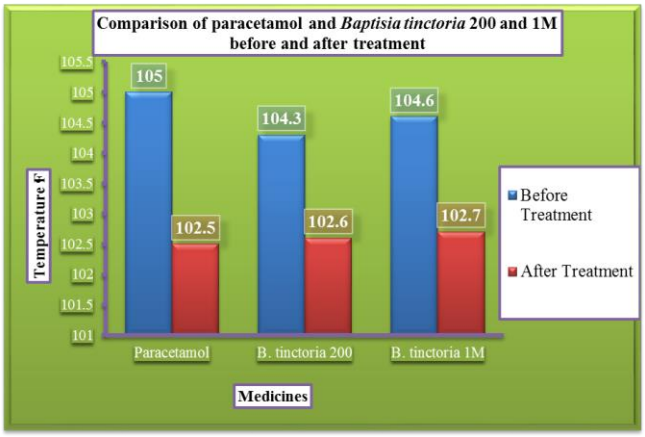

Figure 1. Comparison of paracetamol and *B. tinctoria* 200C and 1M before and after treatment.

Table 2. Antipyretic effects of homeopathic ultrahigh dilutions.

No.	Treatment	Rectal Temperature °F		Rectal Temperature °F after Medicine Administration					
Groups	**Dose**	**0 hour**	**4th hour**	**1st hour**	**2nd hour**	**3rd hour**	**4th hour**	**5th hour**	**6th hour**
Negative Control 90% Ethanol (Vehicle)	Five drops	102.6± 0.31	104.1± 0.26	104.8± 0.26	104.8± 0.30	104.9± 0.29	104.9± 0.22	104.3± 0.31	103.6± 0.31
Paracetamol	150 mg/kg	102.2± 0.86	105.0± 0.50	103.0± 0.31**	102.8± 0.30***	103.4± 0.50**	103.4± 0.49**	102.7± 0.26***	102.5± 0.26**
Baptisia tinctoria 1M	Five drops	102.7± 0.25	104.6± 0.25	104.1± 0.22	103.9± 0.06*	102.9± 0.28***	102.7± 0.23***	102.8± 0.27***	102.7± 0.24*
Baptisia tinctoria 200C	Five drops	102.6± 0.22	104.3± 0.26	103.8± 0.47	103.7± 0.17**	103± 0.31***	102.4± 0.56***	103± 0.25**	102.6± 0.16*

Note: *p ≤0.05, **p ≤0.01, ***p ≤ 0.001 compared to negative control. The data is represented as Mean ± S.E.M N=6, Reading at 0 hour is temperature before *S. cerevisae* injection, 4th hour reading is after fever induction, afterwards hourly readings are after medicine administration reading.

DISCUSSION

B. tinctoria ultrahigh dilutions reduced *S. cerevisiae* induced pyrexia significantly as compared to paracetamol. Baker's yeast causes fever by releasing prostaglandin [9] and antipyretics decrease temperature by reducing PG [17, 18]. Paracetamol 150 mg/kg by oral route reduced *S. cerevisiae* induced pyrexia sufficient to reach statistical significance. Paracetamol act by acting on cyclooxygenase [19]. Other studies also depicts similar findings [3, 13, 20].

Homoeopathic medicine *B. tinctoria* reduced baker's yeast induced fever so it can be assumed that these medicines could play role in reducing PG and cytokine production. However, homeopathic medicines are hypothesized to control inflammation through stimulation of vital force [21]. In selection of homeopathic medicines, not only local symptoms but the whole pathophysiological characteristic symptoms are considered [7, 21]. In homeopathy, the similarity between drug-specific pathogenesis 'remedy picture' and disease-specific individual status is a crucial factor in cure [22]. *B. tinctoria* is a remedy for blood poisons and septic states with low grade fever [8]. In current study, it reduced temperature significantly in few hours, but the effect was not permanent, nor strong. *S. cerevisiae* caused high grade fever during the study. Lack of complete similarity between disease condition and remedy picture might be responsible for slow decreasing of temperature by *B. tinctoria* ultrahigh dilutions as compared to paracetamol. Some other studies described the slow antipyretic effect of *A. napellus* and Typhoidinum against *S. cerevisiae* induced pyrexia due to lack of similarity of causative factor [3, 5]. The effects of *B. tinctoria* ultrahigh dilutions should be evaluated on *Salmonella typhi* induced fever as it has more similarity with typhoid fever type. It can be hypothesized that medicine will be more effectively work in *S. typhi* induced fever due to low grade fever similarity. Moreover, previous studies showed *Nux vomica* and *Pyrogenium* as effective remedies in *S. cerevisiae* induced pyrexia on the basis of some similarity of these medicines with *S. cerevisiae* induced pyrexia [4, 6]. It is poorly understood that how these medicines work however these medicines exert effects in experimental models and clinical trials [23, 24].

CONCLUSION

In conclusion, homoeopathic medicine *B. tinctoria* has weak but significant antipyretic effect against *S. cerevisiae* induced pyrexia, however, it could be important alternative antipyretic when criteria of similarity is met. Homeopathic medicines worked well when criteria of similarity met entirely. If there is a partial similarity, then results are slower or sometimes none.

REFERENCES

1. Saper CB, Breder CD, Flier JS, Underhill LH. The neurologic basis of fever. N Engl J Med. 1994;330(26):1880-6.
2. Minamisawa H, Smith ML, Siesjö BK. The effect of mild hyperthermia and hypothermia on brain damage following 5, 10, and 15 minutes of forebrain ischemia. Ann Neurol. 1990;28(1):26-33.
3. Ahmad S, Rehman T, Abbasi WM. Effect of homoeopathic ultrahigh dilutions of *Aconitum napellus* on Baker's yeast induced fever in rabbits. J Integr Med. 2017;15(3):209-13.
4. Ahmad S, Rehman T, Abbasi WM. In vivo evaluation of antipyretic effects of some homeopathic ultra-high dilutions on Baker's yeast-induced fever on Similia principle. J-AIM. 2018;9:177-82.
5. Ahmad S, Rehman T, Ababsi WM. In vivo evaluation of antipyretic effects of homoeopathic ultrahigh dilutions of Typhoidinum on baker's yeast-induced fever in comparison with Paracetamol. Indian J Res Homoeopathy. 2017;11(3):170.
6. Ahmad S, Abbasi WM, Rehman T. Evaluation of antipyretic activity of Belladonna and Pyrogenium ultrahigh dilutions in induced fever model. J Complement Integr Med. 2018;16(1). pii: /j/jcim.2019.16.issue-1/jcim-2018-0127/jcim-2018-0127.xml.
7. Abbasi W. Concept of Health and Disease in Homeopathy. Int J Complement Alt Med. 2017;8(2):00253.
8. Kent JT. Lectures on materia medica. India: B. Jain Publishers; 2002. p. 803-9.
9. Ataŏglu H, Dŏgan MD, Mustafa F, Akarsu ES. Candida albicans and Saccharomyces cerevisiae cell wall mannans produce fever in rats: role of nitric oxide and cytokines. Life Sci. 2000;67(18):2247-56.
10. Bruguerolle B, Roucoules X. Time-dependent changes in body temperature rhythm induced in rats by brewer's yeast injection. Chronobiol Int 1994;11(3):180-6.
11. Tomazetti J, Ávila DS, Ferreira APO, Martins JS, Souza FR, Royer C, *et al*. Baker yeast-induced fever in young rats: Characterization and validation

of an animal model for antipyretics screening. J Neurosci Methods. 2005;147(1):29-35.

12. Nagase T, Mikami T, Suzuki S, Suzuki M. Pyrogenicity of yeast mannans in rabbits. Microbiol Immunol. 1984;28(6):651-7.
13. Sultana S, Akhtar N, Asif HM. Phytochemical screening and antipyretic effects of hydro-methanol extract of Melia azedarach leaves in rabbits. Bangladesh J Pharmacol. 2013;8(2):214-7.
14. Aziz A, Khan IA, Munawar SH, Sadr-ul-Shaheed S-u-S. Antipyretic study of methanolic bark extract of plumeriarubra, linn. in various pyrexia induced models. Int J Res Dev Pharm Life Sci. 2013;2(6):680-885.
15. Hossain E, Mandal SC, Gupta J. Phytochemical screening and in-vivo antipyretic activity of the methanol leaf-extract of Bombax malabaricum DC (Bombacaceae). Trop J Pharm Res. 2011;10(1):1-6.
16. Adiukwu P, Kayanja F, Nambatya G, Rugera S, Ezeonwumelu J, Tanayen J, *et al*. Antipyretic and Antinociceptive properties o the aqueous extract and Saponin from an edible vegetable: Vernonia Amygdalina leaf. AJFAND. 2013;13(2):7587-606.
17. Jongchanapong A, Singharachai C, Palanuvej C, Ruangrungsi N, Towiwat P. Antipyretic and antinociceptive effects of Ben-Cha-Lo-Ka-Wi-Chian remedy. J Health Res. 2010;24(1):15-22.
18. Ahmad S, Hassan A, Abbasi WM, Rehman T. Phytochemistry and pharmacological potential of Cassia absus–a review. J Pharm Pharmacol. 2018;70:27–41.
19. Flower R, Vane J. Inhibition of prostaglandin synthetase in brain explains the anti-pyretic activity of paracetamol (4-acetamidophenol). Nature. 1972;240(5381):410-1.
20. Abbasi WM, Ahmad S, Perveen S, Rehman T. Preliminary phytochemical analysis and in vivo evaluation of antipyretic effects of hydromethanolic extract of *Cleome scaposa* leaves. eJTCM. 2018;8(1):147-9.
21. Conforti A, Bellavite P, Bertani S, Chiarotti F, Menniti-Ippolito F, Raschetti R. Rat models of acute inflammation: a randomized controlled study on the effects of homeopathic remedies. BMC Complement Altern Med. 2007;7(1):1.
22. Hahnemann S. Essay on a new principle for ascertaining the curative powers of drugs. Hufelands J. 1796;2(part ii):295-352.
23. Ahmad S, Rehman T, Abbasi WM. Homoeopathic approach for the treatment of cancer. Indian J Res Homoeopathy. 2018;12(3):157-63.
24. Shaffique S, Ahmad S, Rehman T, Anwar H, Asif HM, Hussain G, *et al*. Antihyperuricemic activity of gum of Calophyllum inophyllum ultra high dilutions in potassium oxonate induced wister albino rats. IJTK. 2019;18(2):356-9.