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# PHARMACOLOGICAL EVALUATION OF ANTI-PYRETIC ACTIVITY OF SANTALUM ALBUM LEAVES EXTRACT IN WISTAR RATS

**[1]Monika Malviya, [2]Jagdish Chandra Rathi, [3]Shivani Suryavanshi**

**[1,23]NRI INSTITUTE OF PHARMACEUTICAL SCIENCES, BHOPAL, M.P.**

**ABSTRACT:** The main objective of present work is pharmacological evaluation of anti-Pyretic activity of santalum album leaves extract in wistar rats. Phytochemical analysis of methanolic extract of Santalum album showed the presence of alkaloids, carbohydrate, saponins, glycoside and saponin. Quantitative phytochemical assay was performed by calculating total phenolic content (TPC) and total flavonoid content (TFC). The TPC was calculated with respect to gallic acid (standard) and TFC was then calculated with respect to rutin taken as standard. DPPH radical scavenging activity of Santalum album extract exhibited percent inhibition 60.28% and its IC 50value was found to be 48.74µg/ml. Ascorbic was used as a reference compound which exhibited percent inhibition 85.67% and showed IC 50 value of 21.77µg/ml. In the acute toxicity study, no signs of toxicity were found upto the dose of 2000 mg/kg body weight. Hence 1/10th and 1/5th doses i.e. 100 mg/kg and 200 mg/kg have been fixed for study. Brewer's yeast was used to induce fever in albino rats. Fever was recorded 18 hrs after yeast injection since yeast takes a total of about 18 hrs to cause the elevation of body temperature. Subcutaneous injection of Brewer's yeast induces pyrexia by increasing the synthesis of prostaglandin. It is considered as a useful test for the screening of plants materials as well as synthetic drugs for their antipyretic effect. The inhibition of prostaglandin synthesis could is the possible mechanism of antipyretic action as that of paracetamol and the inhibition of prostaglandin can be achieved by blocking the cyclo-oxygenase enzyme activity. Thus it can be postulated that Santalum album, contained pharmacologically active principles that interfere with the release of prostaglandins. After four hours of the test period, the methanolic extract of Santalum album produced appreciable antipyretic activityagainst brewer's yeast induced pyrexia in albino rat. It was revealed that the extract showed dose dependent antipyretic activity. It was revealed that the extractshowed dose dependent antipyretic activity since 100mg/kg dose of test solution is considered as a slow acting compared to the higher dose preparation . This effect may be related to the extract's analgesic and anti-inflammatory activity. There is evidence to believe thatthis plant contains compounds acting as NSAI drugs.

**KEYWORDS:** Antipyretic, Medicines, Pyrexia, Extraction, Assay.

## INTRODUCTION

India is known for its traditional medicinal systems—Ayurveda, Siddha, and Unani. Medical systems are found mentioned even in the ancient Vedas and other scriptures. The Ayurvedic concept appeared and developed between 2500 and 500 BC in India. The literal meaning of Ayurveda is "science of life," because ancient Indian system of health care focused on views of man and his illness. It has been pointed out that the positive health means metabolically well- balanced human beings. Ayurveda is also called the "science of longevity" because it offers a complete system to live a long healthy life. It offers programs to rejuvenate the body through diet and nutrition. It offers treatment methods to cure many common diseases such as food allergies, which have few modern treatments. However, one should be aware that Ayurvedic nutrition is not a "magic bullet" system but requires the full participation of the patient to succeed. It is an interactive system that is user-friendly and educational. It teaches the patient to become responsible and self-empowered. Ayurveda is not a nutritional system for those seeking an escape or excuse to further abuse their body or mind. It is a system for empowerment, a systemof freedom, and long life**.**

Alternative medicines are being used by about 60 percent of the world's population. These medicines are not only used by the rural masses for their primary health care in developing countries but are also used in developed countries where modern medicines dominate. The Indian subcontinent is a vast repository of medicinal plants that are used in traditional medical treatments. The alternative medicines in the traditional systems are derived from herbs, minerals, and organic matter, while for the preparation of herbal drugs only medicinal plants are used. Use of plants as a source of medicine has been an ancient practice and is an important component of the health care system in India. In India, about 70 percent of rural population depends on the traditional Ayurvedic system of medicine. Most healers/practitioners of the traditional systems of medicine prepare formulations by their own recipes and dispense to the patients. In the Western countries, approximately 40 per cent of people are using the herbal medicine for the treatment of various diseases. This interest in traditional medicines is growing rapidly due to the attention being given to it by the governmental agencies and different NGO comprises of general public and researchers as well as the increased side effects, adverse drug reactions, and cost factor of the modern medicines**.** India is the largest producer of medicinal plants. There are currently about 250,000 registered medical practitioners of the Ayurvedic system, as compared to about 700,000 of the modern medicine. In India, around 20,000 medicinal plants have been recorded; however, traditional practitioners use only 7,000–7,500 plants for curing different diseases. The proportion of use of plants in the different Indian systems of medicine is Ayurveda 2000, Siddha 1300, Unani 1000, Homeopathy 800, Tibetan 500, Modern 200, and folk 4500. In India, around 25,000 effective plant-based formulations are used in traditional and folk medicine. More than 1.5 million practitioners are using the traditional medicinal system for health care in India. It is estimated that more than 7800 manufacturing units are involved in the production of natural health products and traditional plant-based formulations in India, which requires more than 2000 tons of medicinal plant raw material annually. More than 1500 herbals are

sold as dietary supplements or ethnic traditional medicines. Alternative medicines are being used by those people who do notuse or cannot be helped by conventional medicinal system**.**

Plants had been used for medicinal purposes long before recorded history. Ancient Chinese and Egyptian papyrus writings describe medicinal uses for plants as early as 3,000 BC. Indigenous cultures (such as African and Native American) used herbs in their healing rituals, while others developed traditional medical systems (such as Siddha, Ayurveda, Unani and TCM) in which herbal therapies were used. The consumption of plant-based medicines and other botanicals in the West has increased manifold in recent years. About two centuries ago, our medicinal practices were largely dominated by plant-based medicines. However, the medicinal useof herbs went into a rapid decline in the West when more predictable synthetic drugs were made commonly available. In contrast, many developing nations continued to benefit from the rich knowledge of medical herbalism. For example, Siddha & Ayurveda medicines in India, Kampo Medicine in Japan, traditional Chinese medicine (TCM), and Unani medicine in the Middle East and South Asia are still used by a large majority of people**.**

Nature always stands as a golden mark to exemplify the outstanding phenomena of symbiosis. Natural products from plant, animal and minerals have been the basis of the treatment of human disease. Today estimate that about 80 % of people in developing countries still relays on traditional medicine based largely on species of plants and animals for their primary health care.

Herbal medicines are currently in demand and their popularity is increasing day by day. About 500 plants with medicinal use are mentioned in ancient literature and around 800 plants have been used in indigenous systems of medicine. India is a vast repository of medicinal plants that are used in traditional medical treatments. The various indigenous systems such as Siddha, Ayurveda, Unani and Allopathy use several plant species to treat different ailments. The use of herbal medicine becoming popular due to toxicity and side effects of allopathic medicines.

## MATERIAL AND METHOD

**List of reagent and chemicals used**

**Table 1: list of reagent and chemicals**

| S. No. | Reagents and chemicals | Company Name |
|---|---|---|
| 1. | Glacial Acetic Acid | Merck |
| 2. | Petroleum ether | Researchlab |
| 3. | Conc. $H_2SO_4$ | Fizmerck |
| 4. | Ethanol | Molychem |
| 5. | Nitroprusside | Merck |
| 6. | Sodium Hydroxide | Merck |

**Table 2: List of glassware's**

| S.No. | Glassware | Company Name |
|---|---|---|
| 1. | Beakers | Borosilicate |
| 2. | Glass rod | Borosilicate |
| 3. | Volumetric flask | Borosilicate |
| 4. | Graduated pipette | Borosilicate |
| 5. | Test tubes | Borosilicate |

**Plant collection**

The medicinal plant Santalum album (300 gm) was collected. After cleaning, plant part (leaves) were dried under shade at room temperature for 3 days and then in oven dried at 45°C till complete dryness. Dried plant part (leaves) was stored in air tight glass containers in dry and cool place to avoid contamination and deterioration.

Authentication of selected traditional plant - Medicinal plant Santalum album was authenticated by a plant taxonomist in order to confirm its identity and purity.

**Extraction**

In present study, plant material was extracted by continuous hot percolation method using Soxhlet apparatus. Powdered material of Santalum album was placed in thimble of soxhlet apparatus. Soxhlation was performing at 60°C using petroleum ether as non-polar solvent. Exhausted plant material (marc) was dried and afterward re-extracted with methanol solvent. For each solvent, soxhlation was continued till no visual colour change will observed in siphon tube and completion of extraction were confirmed by absence of any residual solvent, when evaporated. Obtained extracts was evaporate using rotary vacuum evaporator (Buchitype) at 40°C. Dried extract was weighed and percentage yield for each extract.

## RESULTS AND DISCUSSION

**Percentage Yield**

In phytochemical extraction the percentage yield is very crucial in order to determine the standard efficiency of extraction for a specific plant, various sections of the same plant or different solvents used. The yield of extracts received from the Santalum album is shown in Table 3

**Table 3: Percentage Yield of crude extracts of Santalum album extract**

| S.no | Plant name | Solvent | Theoretical weight | Yield(gm) | % yield |
|---|---|---|---|---|---|
| 1 | Santalum album | Pet ether | 289.23 | 1.59 | 0.54% |
| 2 | | Methanol | 299 | 6.20 | 2.07% |

**Preliminary Phytochemical study**

**Table 4: Phytochemical testing of extract**

| S. No. | Experiment | Presence or absence of phytochemical test | |
|---|---|---|---|
| | | Pet. Ether extract | Methanolic extract |
| 1. | **Alkaloids** | | |
| 1.1 | Dragendroff's test | Present | Present |
| 1.2 | Mayer's reagent test | Present | Present |
| 1.3 | Wagner's reagent test | Present | Present |
| 1.3 | Hager's reagent test | Present | Present |
| 2. | **Glycoside** | | |
| 2.1 | Borntrager test | Absent | Present |
| 2.2 | Killer-Killiani test | Absent | Present |
| 3. | **Carbohydrates** | | |
| 3.1 | Molish's test | Absent | Present |
| 3.2 | Fehling's test | Absent | Present |
| 3.3 | Benedict's test | Absent | Present |
| 3.4 | Barfoed's test | Absent | Present |
| 4. | **Flavonoids** | | |
| 4.1 | Borntragers Test | Absent | Absent |
| 5. | **Tannin and Phenolic Compounds** | | |
| 5.1 | Ferric Chloride test | Absent | Absent |
| 5.2 | Gelatin Test | Absent | Absent |
| 5.3 | Lead Acetate Test | Absent | Absent |

| | | | |
|---|---|---|---|
| 6. | **Saponin** | | |
| 6.1 | Froth Test | Present | Present |
| 6. | **Test for Triterpenoids and Steroids** | | |
| 6.1 | Salkowski's test | Absent | Absent |
| 6.2 | Libbermann-Burchard's test | Absent | Absent |

**Quantitative Analysis**

Preliminary phytochemical testing of crude extracts confirmed the presence of phenolics and flavonoids in plant material. To estimate their amount total phenolic (TPC) and total flavonoid content (TFC) assays were performed.

**Total Phenolic content (TPC) estimation**

**Table 5: Standard table for Gallic acid**

| S. No. | Concentration (µg/ml) | Absorbance |
|---|---|---|
| 1. | 20 | 0.146 |
| 2. | 40 | 0.177 |
| 3. | 60 | 0.195 |
| 4. | 80 | 0.231 |
| 5. | 100 | 0.276 |

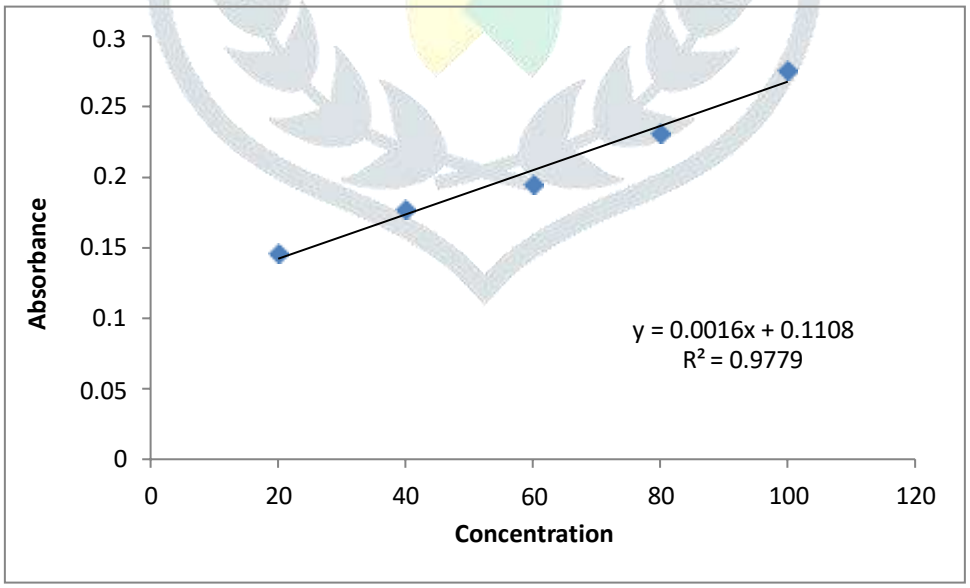



**Figure 1: Represent standard curve of Gallic acid**

**Total Phenolic Content in extract**

**Table 6: Total Phenolic Content**

| S. No | Absorbance | TPC in mg/gm equivalent of Gallic Acid |
|---|---|---|
| 1 | 0.134 | 57.66 mg/gm |
| 2 | 0.177 | |
| 3 | 0.192 | |

**Table 7: Total Phenolic Content of extract Santalum album**

| Extracts | Total Phenolic content (mg/gm equivalent of Gallic acid) |
|---|---|
| Methanol | 57.66 mg/gm |

**Total Flavonoids content (TFC) estimation**

**Table 8: Standard table for Rutin**

| S. No. | Concentration (µg/ml) | Absorbance |
|---|---|---|
| 1. | 20 | 0.176 |
| 2. | 40 | 0.201 |
| 3. | 60 | 0.278 |
| 4. | 80 | 0.315 |
| 5. | 100 | 0.330 |

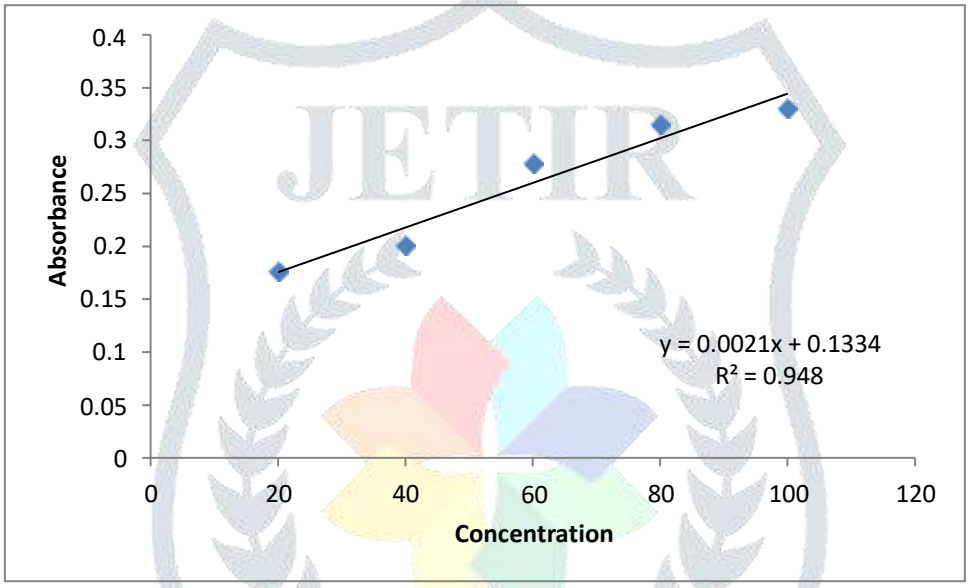



**Figure 2: represent standard curve of Rutin**

**7.3.1.1 Total Flavonoid Content in extractTable 9**:

**Total Flavonoid Content**

| S. No | Absorbance | TFC in mg/gm equivalent of Rutin |
|---|---|---|
| 1 | 0.148 | 17 mg/gm |
| 2 | 0.161 | |
| 3 | 0.192 | |

**Table 10**: **Total Flavonoid Content of extract Santalum album**

| **Extracts** | **Total Flavonoid content (mg/gm equivalent of rutin)** |
|---|---|
| Methanol | 17 mg/gm |

**In vitro Antioxidant Assays**

In the present investigation, the in vitro anti-oxidant activity of extracts of Santalum album was evaluated by DPPH radical scavenging activity. The results are summarized in Tables

**DPPH 1, 1- diphenyl-2-picryl hydrazyl Assay**

**Table 11: DPPH radical scavenging activity of Std. Ascorbic acid**

| **Concentration (µg/ml)** | **Absorbance** | **% Inhibition** |
|---|---|---|
| 20 | 0.483 | 51.261 |
| 40 | 0.439 | 55.701 |
| 60 | 0.347 | 64.984 |
| 80 | 0.280 | 71.745 |
| 100 | 0.142 | 85.671 |
| Control | 0.991 | |
| IC50 | | 21.77 |

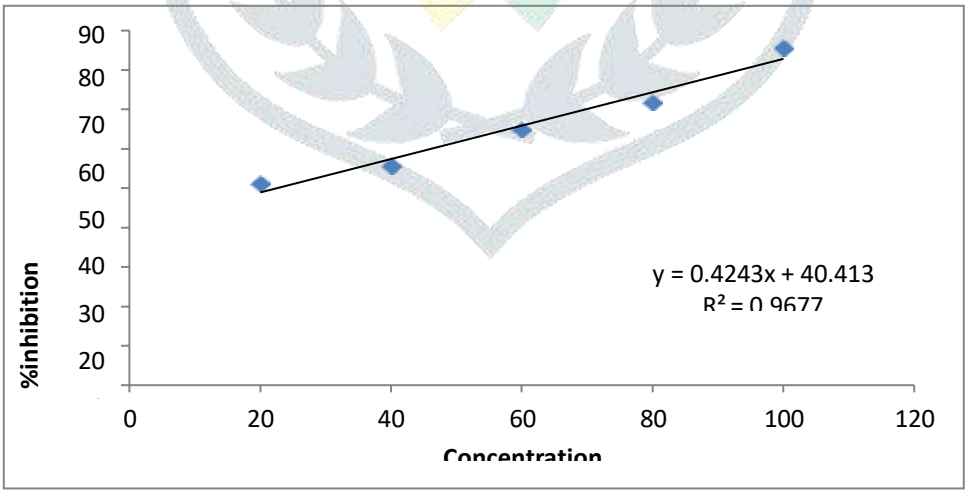



**Figure 3: DPPH radical scavenging activity of Std. Ascorbic acid Table 10:**

**DPPH radical scavenging activity of methanol extract of Santalum album**

| Concentration (µg/ml) | Absorbance | % Inhibition |
|---|---|---|
| 20 | 0.519 | 43.831 |
| 40 | 0.463 | 49.891 |
| 60 | 0.455 | 50.757 |
| 80 | 0.416 | 54.978 |
| 100 | 0.367 | 60.281 |
| Control | 0.924 | |
| IC50 | | 48.74 |

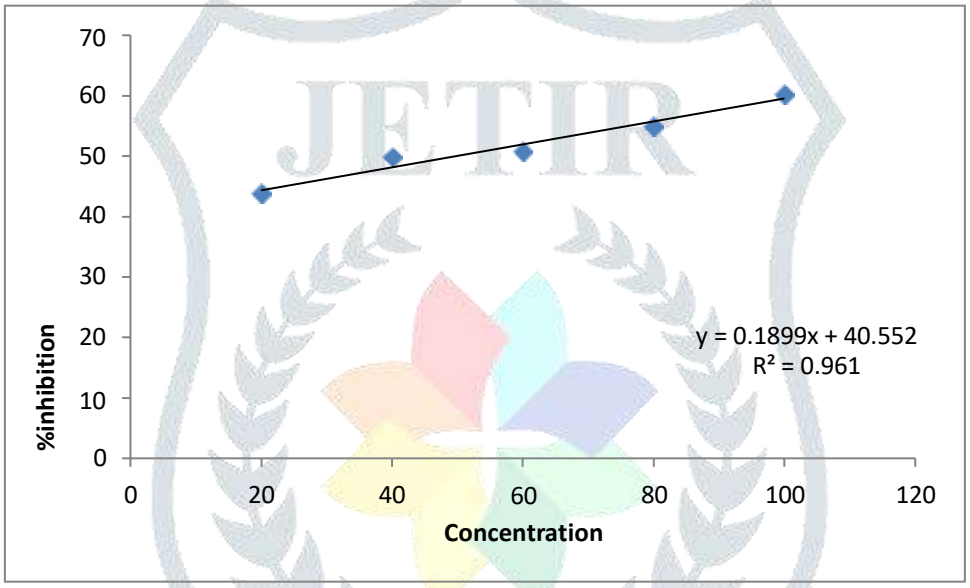
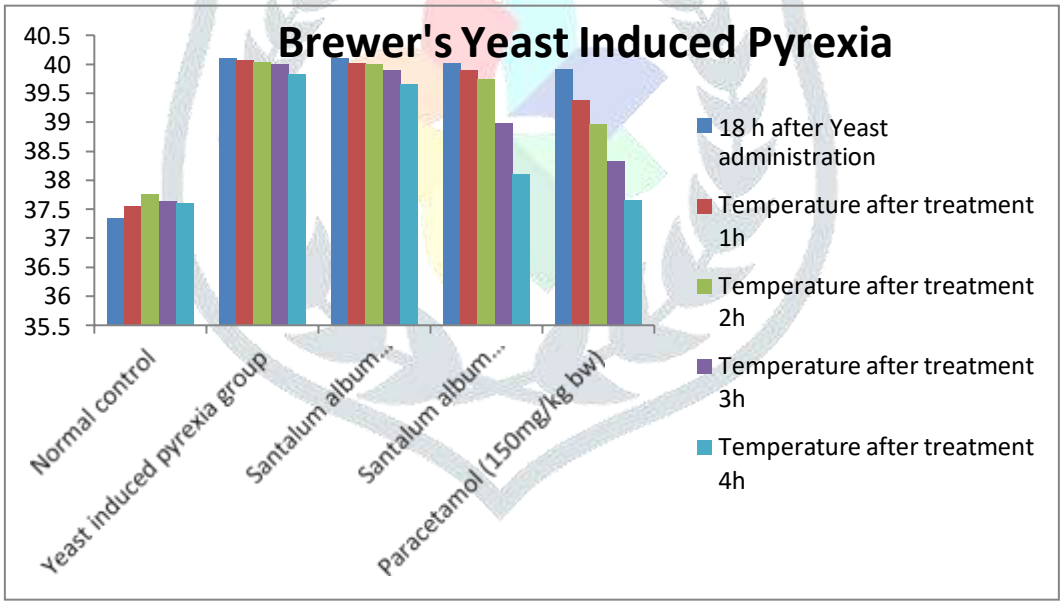



**Figure 4: represents the Percentage Inhibition Vs Concentration of extract of Santalum album**

**Brewer's Yeast Induced Pyrexia in Rats**

**Table 11: Brewer's Yeast Induced Pyrexia in Rats**

| Rectal temperature (°C) | | | | | |
|---|---|---|---|---|---|
| **Groups** | **18 h after Yeast administration** | **Temperature after treatment** | | | |
| | | **1h** | **2h** | **3h** | **4h** |
| Normal control | 37.34±0.1 | 37.56±0.2 | 37.75±0.1 | 37.65±0.2 | 37.60±0.1 |
| Yeast induced pyrexia group | 40.11±0.1 | 40.07±0.3 | 40.03±0.2 | 39.99±0.1 | 39.82±0.3 |
| Santalum album extract(100mg/kg) | 40.10±0.1 | 40.02±0.3 | 39.99±0.1 | 39.91±0.2 | 39.65±0.3 |
| Santalum album extract(200mg/kg) | 40.02±0.1 | 39.91±0.1 | 39.74±0.2 | 38.98±0.1 | 38.11±0.2 |
| Paracetamol (150mg/kg bw) | 39.92±0.2 | 39.39±0.2 | 38.97±0.2 | 38.33±0.1 | 37.66±0.2 |




**Graph 1: Brewer's Yeast Induced Pyrexia in Rats**

## SUMMARY AND CONCLUSION

Phytochemical analysis of methanolic extract of Santalum album showed the presence of alkaloids, carbohydrate, saponins, glycoside and saponin. Quantitative phytochemical assay was performed by calculating total phenolic content (TPC) and total flavonoid content (TFC). The TPC was calculated with respect to gallic acid (standard) and TFC was then calculated with respect to rutin taken as standard. Results shown in Table 8 & table11. DPPH radical scavenging activity of Santalum album extract exhibited percent

inhibition 60.28% and its IC 50value was found to be 48.74µg/ml. Ascorbic was used as a reference compound which exhibited percent inhibition 85.67% and showed IC 50 value of 21.77µg/ml.

In the acute toxicity study, no signs of toxicity were found upto the dose of 2000 mg/kg body weight. Hence 1/10th and 1/5th doses i.e. 100 mg/kg and 200 mg/kg have been fixed for study. Brewer's yeast was used to induce fever in albino rats. Fever was recorded 18 hrs after yeast injection since yeast takes a total of about 18 hrs to cause the elevation of body temperature. Subcutaneous injection of Brewer's yeast induces pyrexia by increasing the synthesis of prostaglandin. It is considered as a useful test for the screening of plants materials as well as synthetic drugs for their antipyretic effect. Yeast induced pyrexia is called pathogenic fever and its etiology could be the production of prostaglandins. The inhibition of prostaglandin synthesiscould is the possible mechanism of antipyretic action as that of paracetamol and the inhibition of prostaglandin can be achieved by blocking the cyclo-oxygenase enzyme activity. There are several mediators for pyrexia and the inhibitions of these mediators are responsible for the antipyretic effect. The oral administration of Santalum album significantly attenuated rectal temperature of yeast induced albino rats. Thus it can be postulated that Santalum album, contained pharmacologically active principles that interfere with the release of prostaglandins. After four hours of the test period, the methanolic extract of Santalum album produced appreciable antipyretic activity against brewer's yeast induced pyrexia in albino rat. It was revealed that the extract showed dose dependent antipyretic activity. The study showed the extract of Santalum album leaves possessed antipyretic effect in yeast induced elevation of body temperature in experimental rats. It was revealed that the extract showed dose dependent antipyretic activity since 100mg/kg dose of test solution is considered as a slow acting compared to the higher dose preparation . This effect may be related to the extract's analgesic and anti-inflammatory activity. There is evidence to believe that this plant contains compounds acting as NSAI drugs. These findings provided strong arguments and validation of the popular use of this plant as antipyretic herb.

## REFERENCES


- Agarwal, A. (2005). Critical issues in quality control of herbal products. Pharma times, 37(6), 09-11.
- Ames, N. J., Peng, C., Powers, J. H., Leidy, N. K., Miller-Davis, C., Rosenberg, A., & Wallen, G. R. (2013). Beyond intuition: patient fever symptom experience. Journal of pain and symptom management, 46(6), 807-816.
- Ampofo, J. A., Andoh, A. H., Tetteh, W., & Bello, M. (2012). Microbiological profile of some Ghanaian herbal preparations: safety issues and implications for the health professions.
- Arunachalam, L. G., Rajendran, K., Mandal, A. B., & Bhattacharya, S. K. (2005). Antipyretic activity of Alstonia macrophylla Wall ex A. DC: An ethnomedicine of Andaman Islands. Pharm Pharm Sci, 8, 558-564.
- Ballabh, B., & Chaurasia, O. P. (2007). Traditional medicinal plants of cold desert Ladakh- Used in treatment of cold, cough and fever. Journal of ethnopharmacology, 112(2), 341-349.

- Borchers, A. A. (2015). Handbook of signs & symptoms. Wolters Kluwer.
- Carapetis, J. R., Beaton, A., Cunningham, M. W., Guilherme, L., Karthikeyan, G., Mayosi, B. M., & Zühlke, L. (2016). Acute rheumatic fever and rheumatic heart disease. Nature reviews Disease primers, 2(1), 1-24.
- Diehl, K. A., Crawford, E., Shinko, P. D., Tallman Jr, R. D., & Oglesbee, M. J. (2000). Alterations in hemostasis associated with hyperthermia in a canine model. American journal of hematology, 64(4), 262-270.
- Emmerton, L., Chaw, X. Y., Kelly, F., Kairuz, T., Marriott, J., Wheeler, A., & Moles, R. (2014). Management of children's fever by parents and caregivers: Practical measurement of functional health literacy. Journal of Child Health Care, 18(4), 302-313.
- Evans, S. S., Repasky, E. A., & Fisher, D. T. (2015). Fever and the thermal regulation of immunity: the immune system feels the heat. Nature Reviews Immunology, 15(6), 335-349.
- Geneva, I. I., Cuzzo, B., Fazili, T., & Javaid, W. (2019, April). Normal body temperature: a systematic review. In Open forum infectious diseases (Vol. 6, No. 4, p. ofz032). US: Oxford University Press.
- Heilman, J. M., De Wolff, J., Beards, G. M., & Basden, B. J. (2014). Dengue fever: a Wikipedia clinical review. Open medicine, 8(4), e105.
- Kiekkas, P., Aretha, D., Bakalis, N., Karpouhtsi, I., Marneras, C., & Baltopoulos, G. I. (2013). Fever effects and treatment in critical care: literature review. Australian critical care, 26(3), 130-135.
- Lambert, G. P. (2004). Role of gastrointestinal permeability in exertional heatstroke. Exercise and sport sciences reviews, 32(4), 185-190.
- Leggett, J. (2012). Approach to fever or suspected infection in the normal host. In Goldman's Cecil Medicine (pp. 1768-1774). WB Saunders.
- Leon, L. R. (2002). Invited review: cytokine regulation of fever: studies using gene knockout mice. Journal of Applied Physiology, 92(6), 2648-2655.
- Loeser, J. D. (2001). Bonica's management of pain (Vol. 3). Philadelphia: Lippincott Williams & Wilkins.
- Mackowiak, P. A. (2000). Temperature regulation and the pathogenesis of fever. Principles and practice of infectious diseases, 6, 703-718.
- Megarbane, B., Resiere, D., Shabafrouz, K., Duthoit, G., Delahaye, A., Delerme, S., & Baud, F. (2003). Descriptive study of the patients admitted to an intensive care unit during the heat wave of August 2003 in France. Presse Medicale (Paris, France: 1983), 32(36), 1690-1698.
- Muralidharan, R., & Narasimhan, D. (2012). Ethnomedicinal plants used against gastrointestinal problem in Gingee Hills of Villupuram district, Tamil Nadu. Journal of Applied Pharmaceutical Science, 2(10), 123-125.
- Mustafa, S., Elgazzar, A. H., Essam, H., Gopinath, S., & Mathew, M. (2007). Hyperthermia alters kidney function and renal scintigraphy. American Journal of Nephrology, 27(3), 315- 321.

- Niven, D. J., Laupland, K. B., & Stelfox, H. T. (2016). Accuracy of peripheral thermometers for estimating temperature. Annals of internal medicine, 165(1), 73-74.
- Osterhout, J. A., Kapoor, V., Eichhorn, S. W., Vaughn, E., Moore, J. D., Liu, D. & Dulac, C. (2022). A preoptic neuronal population controls fever and appetite during sickness. Nature, 606(7916), 937-944.
- Pandey, M. M., Rastogi, S., & Rawat, A. K. (2008). Indian herbal drug for general healthcare: an overview. The internet journal of alternative medicine, 6(1), 3.
- Pasero, C., & McCaffery, M. (2010). Pain assessment and pharmacologic management-E- Book. Elsevier Health Sciences.
- Pasero, C., Paice, J. A., & McCaffery, M. (1999). Basic mechanisms underlying the causes and effects of pain. Pain: clinical manual, 15-34.
- Przybyła, G. W., Szychowski, K. A., & Gmiński, J. (2021). Paracetamol–An old drug with new mechanisms of action. Clinical and Experimental Pharmacology and Physiology, 48(1), 3-19.
- Schultz, C. L., Tchume-Johnson, T., Schapira, M. M., Bellamy, S., Smith-Whitley, K., & Ellison, A. (2015). Adherence to prompt fever evaluation in children with sickle cell disease and the health belief model. Pediatric Blood & Cancer, 62(11), 1968-1973.
- Strengell, T., Uhari, M., Tarkka, R., Uusimaa, J., Alen, R., Lautala, P., & Rantala, H. (2009). Antipyretic agents for preventing recurrences of febrile seizures: randomized controlled trial. Archives of pediatrics & adolescent medicine, 163(9), 799-804.
- Subhose, V., Srinivas, P., & Narayana, A. (2005). Basic principles of pharmaceutical science in Ayurvĕda. Bulletin of the Indian Institute of History of Medicine (Hyderabad), 35(2), 83-92.
- Sullivan, J. E., Farrar, H. C., Section on Clinical Pharmacology and Therapeutics, & Committee on Drugs. (2011). Fever and antipyretic use in children. Pediatrics, 127(3), e20103852.
- Teagle, A. R., & Powell, C. V. (2014). Is fever phobia driving inappropriate use of antipyretics. Archives of disease in childhood, archdischild-2013.
- Todd, W. T. A., Lockwood, D. N. J., Nye, F., Wilkins, E., & Carey, P. (2002). Infection and immune failure.
- Trautner, B. W., Caviness, A. C., Gerlacher, G. R., Demmler, G., & Macias, C. G. (2006). Prospective evaluation of the risk of serious bacterial infection in children who present to the emergency department with hyperpyrexia (temperature of 106 F or higher). Pediatrics, 118(1), 34-40.