EXPERIMENTAL EVALUATION OF ANTIPYRETIC EFFECT OF HOMOEOPATHICMEDICINE PYROGENIUM 200, COMPARISON WITH STANDARD PARACETAMOL, IN BAKER'S YEAST INDUCED FEVER IN ALBINO RAT MODEL

A DISSERTATION TO BE SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENT

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BY

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DECLARATION

I, **Dr.Vaishnavi.H** do hereby declare that this dissertation entitled **"EXPERIMENTAL EVALUATION OF ANTIPYRETIC EFFECT OF HOMOEOPATHIC MEDICINE PYROGENIUM 200 COMPARISON WITH STANDARD PARACETOMOL IN BAKER'S YEAST INDUCED FEVER IN ALBINO RAT MODELS"** is a bonafide work carried out by me under the direct supervision and guidance of **Dr. KRISHNA KUMARI AMMA HOD, DEPARTMENT OF MATERIA MEDICA** under the co-guidance of **Dr. WINSTON VARGHEESE MD(HOM) PROFESSOR, DEPARTMENT OF MATERIA MEDICA** in partial fulfillment of the regulation for the award of the degree of **DOCTOR OF MEDICINE(HOM)** in Materia Medica. This work confirms the standards prescribed by **THE TAMILNADU DR.MGR MEDICAL UNIVERSITY, CHENNAI.** This has not been submitted in full or part for the award of any degree or diploma from any university.

Place: Kulasekharam **Dr.VAISHNAVI. H**

Date:

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ABSTRACT

A group of 18 wistar albino rats were induced with fever by inducing Baker's yeast intraperitoneally, then group 1 received normal saline and served as control group, group 2 received Paracetamol 100mg/kg for every 4 hours and group 3 received 5drops of freshly prepared Pyrogenium 200 for 4hourly. And temperature of all the rat models were noted every hourly. General blood parameters were analyzed before and after the administration of drug. And Pyrogenium 200 is found to be effective in controlling fever when compared with the standard paracetamol with respect to the mentioned parameters. The study is statistically significant with a p value <0.5.

Keywords:

Fever, Baker's yeast, Temperature, Blood parameters, Paracetamol, Pyrogenium 200.

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ABBREVATIONS USED

SL.NO	ABBREVATIONS	EXPLANATION
1	Kg	KILOGRAM
2	F	FAHRENHEIT
3	ml	MILILITRE
4	G	GROUP
5	aqua	WATER
6	D	DOSE
7	gtt	DROPS
8	hrly	HOURLY
9	PGE_2	PROSTAGLANDIN E_2
10	IL	INTERLEUKIN
11	TNFα	TUMOUR NECROSIS FACTOR ALPHA
12	C	CENTIGRADE, CELSIUS.
13	RBC	RED BLOOD CELLS
14	WBC	WHITE BLOOD CELLS
15	N	NEUTROPHIL
16	L	LYMPHOCYTE
17	E	EOSINOPHIL
18	M	MONOCYTE

19	HIV	HUMAN IMMUNODEFICIENCY VIRUS
20	BUN	BLOOD UREA NITROGEN
21	CK	CREATINE KINASE
22	UTI	URINARY TRACT NFECTION
23	CSF	CEREBRO SPINAL FLUID
24	IgM	IMMUNOGLOBULIN M
25	EBV	EBSTEIN BARR VIRUS
26	CMV	CYTOMEGALO VIRUS
27	ESR	ERYHROCYTE SEDIMENTATION RATE

1. INTRODUCTION

Fever is an elevated body temperature that is mediated by increase in the hypothalamic heat regulating set point. Fever is the physiological response to infection or inflammation.(1)

The thermoregulatory center receives information from cold and warm receptors of peripheral nerves and temperature ofbloodperfusingarea. Heat is produced by metabolic process and muscular activity. And the excess heat is dissipated through lungs and skin. (2)

Pharmacologic treatment to reduce the fever is through the antipyretic drugs such as aspirin or acetaminophen, 325-650mg every 4 hours. (3)

In homoeopathy the medicine Pyrogenium has a great action in reducing the fever and the associated symptoms in the patients. So, this experimental study is to prove that how much Pyrogenium in 200th potency is effective in reducing fever when compared with the other antipyretic drugs such as acetaminophen through Baker's yeast induced fever in wistar albino rats by monitoring the temperature and by analysing the blood parameters such as Total WBC, platelets, neutrophils , monocytes, lymphocytes.

1.1 BACKGROUND AND JUSTIFICATION OF STUDY

From some experimental studies the antipyretic effect of homoeopathic medicine iscompared with paracetamol and found to be significantly effective in reducingtemperature and the associated symptoms.(4)

In the literatures of homoeopathic Materia Medica, it is found that Pyrogenium has great antipyretic action. In modern medicine paracetamol is used as a standard medicine for treating pyrexia. So through the evidence based study I wish to prove and compare the antipyretic effect of Pyrogenium in 200th potency with paracetamol in baker's yeast induced fever on wistar albino rats. (5)(6)

1.2 SCOPE OF THE STUDY

- There are not much of experimental studies in homoeopathy. This becomes one of the experimental studies in homoeopathy.
- This is an evidence-based study.
- This becomes an experimental model for conducting study on other drugs.
- Authenticity of homoeopathic Materia Medica can be experimentally proved.
- Notion of the current scientific world and layman about homoeopathy research can be changed.
- Unlike clinical trials, experimental study gives an opportunity for publication in journal other than homoeopathic.
- Acceptance by scientific community.
- Gives courage to budding homoeopaths to take up animal experiment.

2. AIMS AND OBJECTIVES

- To study the antipyretic effect of Pyrogenium 200thpotency in fever induced wistar albino rats.
- To study the effectiveness of Pyrogenium 200thpotency in treating fever comparing with Paracetamol.

3. REVIEW OF LITERATURE

3.1 DEFINITION OF FEVER

Fever is an elevation of body temperature above normal circadian variation as a result of the change in the thermoregulatory centre, located in the hypothalamus.[7]

3.2REGULATION OF BODY TEMPERATURE

Body's normal temperature is ordinarily maintained, despite environmental variations, by the hypothalamic thermoregulatory center which balances the excess heat production derived from the metabolic activity in muscles and the liver with heat dissipation from the skin and lungs.

Rapid muscle contractions, increasing metabolism and conserving heat by peripheral vasoconstriction leads to rapid rise in temperature. Heat loss by radiation convection and conduction from the surface is slow. Evaporation of the sweat leads to rapid loss of heat.

Fever occurs when there is increase in the hypothalamic set point for the temperature. Once the set point of hypothalamus is raised neurons in the vasomotor center are get stimulated and cause peripheral vasoconstriction especially in extremities leads to decrease in heat loss from the skin and the person feels cold.

Temperature-decreasing mechanism when the body is too hot is by sweating, vasodilatation of skin blood vessels, sweating, decrease in heat production. Temperature-increasing mechanisms when the body is too cold are by skin vasoconstriction throughout the body, piloerection and by increase in thermogenesis. (8)(9)

3.3NORMAL BODY TEMPERATURE:

The normal mean oral temperature in healthy individuals is said to be 36.8°±0.4°(98.2°±0.7°F), with low level at 6 am and higher levels at4-6pm. The

maximum normal oral temperature is said to be 37.2°(98.9°F) and 36.8°C(99.9°F) at 4pm. These values define the 99th percentile for healthy individuals.

Generally rectal temperature will be 0.4°C (0.7°F) higher than the oral temperature. And in women who menstruate the morning temperature is generally lower in the two weeks before ovulation: then the temperature rises by 1°F with the ovulation and then it remains at that level until the menses occur.

In the post prandial state the body temperature can be elevated. In some conditions can affect the body temperature such as pregnancy and endocrinology dysfunction.

In most patients with increased body temperature have fever, there are circumstances in which raised temperature represents not fever but hyperthermia. Hyperthermia is characterized by an uncontrolled raise in body temperature that exceeds the body's ability to lose heat. The setting of hypothalamic thermoregulatory center is unchanged.[9][10]

3.4 RECORDING OF TEMPERATURE:

Oral temperature is ideal for clinical use in all conscious, cooperative adults and older children. 90 seconds is the minimum equilibrium time with mercury in glass thermometer. Axillary temperature considerably altered by environmental factors so they are less reliable and it is 0.3°C to 0.6°C less than oral temperature. The core temperature is the temperature of the viscera and the inner tissues. The core temperature of the body is about 0.6°C (1°F) higher than the oral temperature of the body. In unconscious patients, patient undergoing intensive care and during major surgery rectal temperature can be measured.[10][8]

1°C=18°F

C- Centigrade also called as Celsius.

0°C corresponds to 32°F

F-Fahrenheit.[8]

3.5 PATHOGENESIS OF FEVER:

Infection is defined as invasion of a pathogen that triggers an immune response, whether the infection is asymptomatic or symptomatic. Manifestation of infection are protean and due to as much to our immune response as to attributes of the particular pathogen. The inflammatory response that accompanies infection is usually marked by fever. Fever is a tightly controlled elevation in body temperature above the normal range in response to a central nervous system change in set point.[11]

Pyrogen is said to be any substance with causes fever. Exogenous pyrogens are derived from outside the patient; most are microbial products, microbial toxins, or whole organisms. The classic example of exogenous pyrogen is lipopolysaccharide (endotoxin) produced by all gram-negative bacteria. Pyrogenic products of gram-positive organisms include the enterotoxins, of staphylococcus aureus and the group A and B streptococcal toxin, also called superantigens. Staphylococcal toxin of clinical importance is that associated with isolates of S.aureus from patients with toxic shock syndrome. These products of staphylococci and streptococci cause fever in experimental animals when injected intravenously at concentration of 1-10μg/kg. The pyrogenic cytokines are small proteins which regulate immune, inflammatory and hematopoietic processes. The pyrogenic cytokines include (interleukin) IL-1,IL6,(Tumour necrotic factor) TNF, Ciliaryneutrophic factor and interferon.[9]

The synthesis and release of pyrogenic cytokines are induced by viruses and also by wide spectrum of bacterial and fungal products. However fever can also be a manifestation of some disease in the absence of microbial infection. In conditions like trauma, tissue necrosis or antigen-antibody complexes, inflammatory processes can

induce the production of IL-1,TNF,IL-6 which individually or in combination trigger the hypothalamus to increase the set point to febrile levels. When the set-point of the hypothalamic temperature-regulating center becomes higher than normal, all the mechanism for raising the body temperature are brought to play, including increased heat production and heat conversation.

At the time of fever the levels of prostaglandin E_2 (PGE_2) are elevated in third cerebral ventricle and hypothalamic tissue. Near the circumventricular vascular organ the networks of enlarged capillaries surrounding the hypothalamic regulatory centers concentration of prostaglandin E_2 elevated. The exogenous and endogenous pyrogens interact with endothelium of these capillaries and that this interaction is the first step in initiating fever. Pyrogenic cytokines such as IL-1,IL-6 and TNF are released from the cells and enters the systemic circulation. Although the systemic effects of these circulating cytokines lead to fever by inducing the synthesis of prostaglandin E_2 they induce PGE_2 in peripheral tissues. For PGE_2 there are four receptors and each signal the cells in different ways. Of the four receptors the third receptor is essential for fever.

Several viral disease cause active infection in the brain. The neuronal cells and glial cells synthesize IL-1,IL-6. Therefore, CNS production of these cytokines apparently can elevate the hypothalamic set point, by passing the circumventricular organs involved in fever caused by circulating cytokines.[9]

In addition to this there will be rise of white blood cells as a part of immune response. [12]

The severity of the fever is classified as;

Low grade (100.5–102.1°F or 38.1–39°C)

Moderate (102.2–104.0°F or 39.1–40°C)

High (104.1–106.0°F to or 40.1-41.1°C)

Fevers that exist for days or weeks with no explanation are called fevers of undetermined origin (FUO) or pyrexia of unknown origin.

Hyperthermia or hyperpyrexia:

It refers to extreme elevation in temperature above 106°F, which could be due to heat stroke, heat exhaustion or malignant hyperpyrexia.[13]

Hypothermia:

It is the abnormally low temperature below 95 °F rectally.[13]

3.5.1 FEVER AS A DEFENSE MECHANISM:

For some microorganisms at least, a febrile host response may assist in terminating the infection and speedy recovery. Experimental studies say that raised body temperature interfere with the virulence factor or the growth of some viral and bacterial pathogens. Fever increases the immune reaction and increases the phagocytic, chemo tactic and bactericidal activity of polymorph nuclear leukocytes. And this febrile response may not seen even in the presence of severe infection in immune compromised individuals and those at the extremes of age. Such persons are at the greater risk in resisting infections.[8]

There are commonly four types of febrile reactions:[14]

Intermittent or septic fever:

It is characterized by daily elevation of temperature with interspersed period of normal body temperature. Intermittent fever is the suggestive of acute bacterial infections, such as acute cystitis, pneumonia etc.

Remittent fever:

In remittent fever the temperature rises and falls everyday but does not return to normal.

Continued or sustained fever:

The rise of temperature is maintained for several days or weeks, and there are only little variations between individual determinations. This type of fever associated in conditions such as military tuberculosis, typhoid, malignancy, endocarditis and in central nervous system lesions.

Relapsing fever:

In relapsing fever the febrile period interspersed between one or several days of normal temperature. This is usually seen in malaria.

Pel-Ebstein'sfever:

It is cyclic fever in which fever lasting for 3 to 10 days alternates with afebrile periods of the same duration.[10]

3.6 CLINICAL FEATURES:

- Feeling hot. Due to the increase in the metabolic rate. The oxygen consumption in the body increases by 13% for each 1°C rise of the body temperature. So this can aggravate the pre-existing cerebrovascular, cardiac or pulmonary insufficiency.
- In the initial stages chills occurs due to vasoconstriction.
- Heart rate increases for every 1°C rise in body temperature above normal range. It increases by 18beats per minute. In rheumatic heart fever and pneumonia it may be disproportionately high and can be said as rapid pulse fever. Slow pulse fever is seen in typhoid, brucellosis, meningitis, drug induced fever and leptospirosis where pulse is disproportionately slow.
- Increased blood pressure- due to vasoconstriction during the period of rise in body temperature.

- Respiratory rate increases during fever. In the ratio 1:4 with the heart rate is maintained except in conditions like pneumonia and pleural effusion.
- Rigor. Shivering occurs with rapid increase in body temperature from any cause. And they are due to vigorous muscle contraction. Recurrent attack of rigor is seen in urinary tract infection, filariasis, malaria and abscess. And in continuous fever treated with antipyretics intermittently, rigor may occur. When the drug effect ceases rigor occurs in an attempt on the part of the body to resume the high body temperature.
- Excessive sweating- almost in all type of fever fall of temperature is accompanied by sweating. Night sweats is the characteristic feature in infective endocarditis, tuberculosis and lymphoma.
- Headache may accompany with any kind of fever but in intracranial infection and sinusitis the prominent and characteristic feature is severe headache with photophobia.
- Delirium- It is common in the very young and old. In organic brain syndrome fever may induce brain changes. The endorphins released in the brain by the effect of cytokines TNFα and IL-1 may precipitate delirium.
- Myalgia- may occur with viral infection such as influenza, enterovirus, dengue fever, leptospirosis and with septicemia, including meningococcal sepsis.
- Shock – it may accompany with severe infection and sepsis. And fluid loss increases due to sweating and evapouration. For 1°C rise of body temperature average of 360ml of excess fluid is needed for 24 hours.
- Herpes labialis- due to the activation of latent viral infection of herpes simplex which causes vesicles in the mucocutaneous junction of nose and lips. It is common on pneumonia and meningitis.[15]

3.7INVESTIGATION:

- A complete blood count with differential count, including eosinophil count.
- Liver function test, urea and electrolytes, blood glucose and muscle enzyme.
- Erythrocyte sedimentation rate, C - reactive protein and inflammatory markers.
- A test for antibodies to HIV-1.
- Auto antibodies, including antinuclear antibodies.
- Chest x-ray and Electrocardiogram.-as identified by clinical considerations.
- Urinalysis and urine culture- pyuria; bacteriuria; crystalluria is seen urinary tract infections.
- Blood culture
- Throat swab for culture
- Electrolytes, blood sugars, BUN, Creatinine, CK, liver function tests mainly help in localizing inflammations and quantifying functional deficits which can be used to monitor therapeutic responses.
- Other specimen, as indicated by examination. Blood culture in sepsis, urine culture in UTI, CSF in meningitis, sputum in pneumonia, pus in abscess.
- Detection of viral/fungal/bacterial antigens in blood or body fluids such as HBsAg in hepatitis B virus.
- Demonstration of parasites like microfilaria and malaria in blood, leishmania in liver and bone marrow specimen, amoeba in stool or from abscess wall scraping.
- Demonstration of antibodies to specific pathogen such as in Widal in typhoid, IgM antibodies against many viruses like hepatitis A, E and dengue virus.

- Tuberculosis, histoplasmosis, sarcodiosis and others can be diagnosed by biopsy of lymph node, liver and other organs through histopathology.
- Leucocyte pattern:

  Neutrophil leukocytosis and presence of juvenile or band form of neutrophils and toxic granulations in the neutrophils usually seen in bacterial infection. In severe sepsis condition there will be increased severity in leukocytosis. Neutrophils more than 70% with the total WBCs above10000/cu mm is the suggestive of pyogenic infection.

  ESR is elevated in multitude of causes and in non infective conditions also. In viral infections, typhoid, brucellosis, leishmaniasis, tuberculosis, histoplasmosis, SLE, infiltrative disease of bone marrow, parvovirus B19mild to moderate neutropenia is seen.

  Lymphocytosis is seen in viral infections. Atypical lymphocytes seen in EBV, CMV, HIV dengue, rubella, measles, varicella, viral hepatitis, serum sickness and toxoplasmosis. Monocytosis is the suggestive of typhoid and tuberculosis. Eosinophilia is the suggestive of parasitic infections, filiariasis, and hypersensitivity to drugs.[16][8][14]

3.8 REMEDY:

PYROGENIUM

SYNONYM:

A product of sepsin.

INTRODUCTION:

Pyrogen is the great remedy for septic states, with intense restlessness. Sepsis is the essence of the action of pyrogen[17]. Pyrogen can said to be the “aconite of typhoid quality of pyrexia”. [17] “In septic fevers, especially puperal, pyrogen has demonstrated its great value as a homeopathic dynamic antiseptic. Hectic, typhoid,

typhus, ptomaine poisoning, course of diphtheria(18), scarlet fever(19), dissecting wounds, sewer-gas poisoning, chronic malaria, after-effects of miscarriage, all these conditions at times may present symptoms calling for this unique medicine. Pyrogenium influenza patients are liable to acute digestive disturbances-entritis rather than gastritis. Acute abdominal pains accompanied by very violent diarrhea, always a very offensive and rather profuse watery stools.[20]

PREPARATION:

A product of the decomposition of chopped lean beef in water, allowed to stand in the sun for two or three weeks. Dilutions, which should be made, according to Burnett, direct and without glycerin.

Pyrogenium was introduced by Dr. Drysdale as far back as 1880. He was struck by the fever-exciting power exerted by the "sepsin" of Panum, the "pyrogen" of Burdon-Sanderson, which was the toxin formed by the bacteria of putrefaction. He inferred that it must also be febrifuge, if only we could define the pyrexia to which it was suitable; and, reasoning somewhat isopathically, concluded that this was such as obtained in septicemia after wounds and in the toxemic fevers generally. "The most summary indication for pyrogen would be," he wrote, "to term it the aconite of the typhus or typhoid quality of pyrexia." He proceeded to act on this inference, and published a paper embodying his views and results in the British Journal of Homoeopathy of the year. Partly from the spoiling of one of his preparations, and partly perhaps from giving the remedy in too low dilution, he was discouraged from proceeding farther; but in 1885 his thought was taken up by Dr. Burnett. In his pamphlet on "Fevers and Blood-poisoning and their treatment, with special reference to the use of Pyrogenium" (1888) he tells us how he was led to test the remedy, preparing it after Drysdale's fashion, but giving it in the 6th dilution. The result of his

experience (some of which he relates) was to assure him that Pyrogenium indeed fills the vacant place of a remedy which acts on the toxemic fevers as effectively as aconite on those of the "inflammatory" type[21].Burnett used chiefly the 6th centesimal dilution, which is perfectly harmless, and which keeps indefinitely. [22]

SPHERE OF ACTION:

Pyrogen predominantly acts on blood, heart, circulation, muscles, gastro intestinal, skin.[24]

PATHOGENY:

It causes septic condition and blood poisoning. It also causes septic fever, typhoid condition, puerperal sepsis and diphtheria.[25]

FEVER:

It is a great remedy for septic fevers, enteric fever, hectic fever, Indian continued fever, influenza. Latent pyogenic condition. Chronic complaints that date back to septic conditions. Great soreness of the body, bed seems hard, constantly moves in search of soft, comfortable position .Great pain and violent burning in abscesses. [21]

Temperature:

Temperature rises rapidly. Feels hot as if he had a fever, but was only 99°F, feels like 105°F. Great heat with profuse hot sweat, but sweating does not cause a fall in temperature. All cases fever commencing with pains in the limbs. Temperature rises rapidly to 104°F and sinks rapidly from heart failure.[26]

Chill:

Coldness and chilliness. Chill begins in the back. Chilly at times and a little aching; bed feels hard. Shivers and begins to move about restlessly. Cold and chill all day. Frequent calls to urinate as soon as fever came on. [26]

Sweat:

Cold sweat over body. Perspiration horribly offensive, carrion-like.[26]

Heart:

Pulse abnormally rapid, out of proportion to the temperature. Palpitation. Tired feeling about the heart. Threatening heart failure in zymotic and septic fevers.

Female:

Fever at each menstrual period, consequent upon latent pelvic inflammation. Septic puerperal infection. Puerperal fever with offensive lochia; septicemia following abortion when fetus or secundines are retained. All discharges are horribly offensive-menstrual, lochial, diarrhea, vomit, sweat, breath etc.[26][17][23]

MODALITIES:

Aggravation:

Cold damp, Motion, Constant change of position, Sitting, Moving eyes.

Amelioration:

Heat, Hot; Bath, drinks, Pressure, Stretching, Changing position, Walking.[26][27][24]

3.9 RELATED ATRICLES :

1) Experimental evaluation of antipyretic and analgesic activities of *AmalakyadiGana*: An Ayurvedic formulation. [6]

2) *In vivo* evaluation of antipyretic effects of homoeopathic ultrahigh dilutions of *Typhoidinum*on baker's yeast-induced fever in comparison with *Paracetamol.* [28]

3) Antipyretic Activity of Abutilon mauritianum (Jacq.) Roots in Wistar Rats [5]

4) In vivo evaluation of antipyretic effects of some homeopathic ultra-high dilutions on Baker's yeast-induced fever on Similia principle.[29]

4.MATERIALS AND METHOD

4.1 STUDY SETTINGS

18 Wistar albino rats are taken for the study. The rats are divided into 3 groups consisting of 6 animals each.The lab setup was made in Cape Bio Lab & Research Centre, CSI Complex, Marthandam – 629165.

4.2 SELECTION OF SAMPLES

Healthy wistar albino rats of either sex about 90 days old, weighing about 150-220g were taken for the study.

4.3 STUDY DESIGN

This is an experimental study on Wistar albino rats with Baker's yeast induced fever.

4.4 INTERVENTION

- Pyrogenium 200thpotency was administered orally in Wistar albino rats respectively. The homoeopathic medicine is given in water dose, 1 drop of Pyrogenium 200dilution is mixed with 10ml of aqua and 5drops, this freshly prepared medicine was administered every four hourly as like the frequency of administration of paracetamol.

4.5 BRIEF OF PROCEDURES

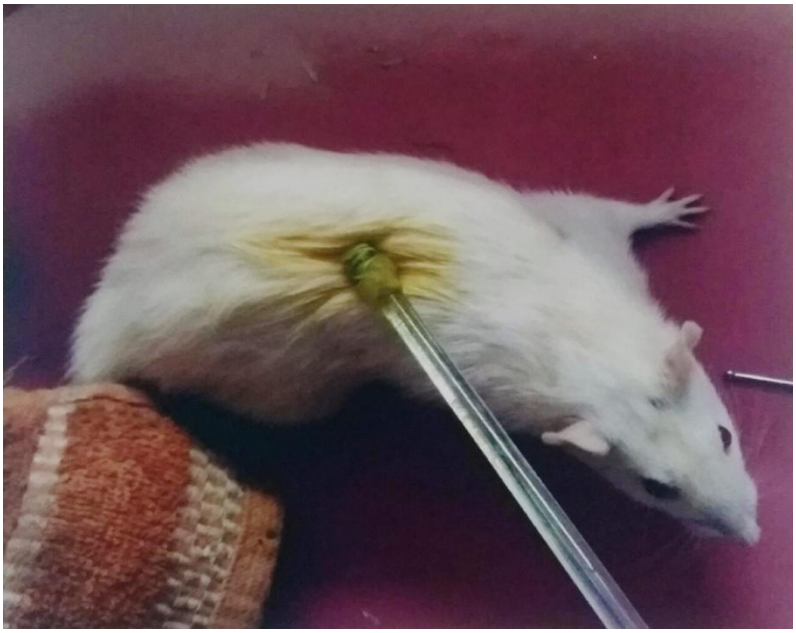
- Wistar albino rats of either male or female weighing about 150-220gm in the same age group of 2 to 3 months old of either sex will be acclimatized to the experimental room at temperature 23+/- 2ºC, controlled humidity conditions (50-55%) and 12hours light/dark cycle for a period of 1 week.
- Animals were caged in a clean polypropylene cage and fed with standard food pellets and water.

- After 1 week of acclimatization the animals are divided randomly into 3 groups, containing 6 animals each.
- Initially the temperatures of all the animals were recorded rectally by using lubricated thermometer before inducing baker's yeast.
- Baker's yeast (saccharomyces cerevisiae)[30] was suspended in normal saline at the dosage of 135mg/kg/10ml [31][30]and induced intraperitoneally in all animals in all the three groups.
- And temperature was noted 4 hours after the yeast injectionrectally with the lubricated thermometer. (30)
- The animals showing ≥0.5F◦-1.5 F◦ raise of temperature was taken for the study.
- Group 1 - received vehicle (0.9% saline) orally and served as control group.
- Group 2 - was treated with paracetamol (100mg/kg) orally for every 4 hourly by oral feeding needle.
- Group 3 –was treated with 5 drops of freshly prepared Pyrogenium 200th potency orally for every 4 hourly by oral feeding needle.(Dr. Willmar Schwabe homoeopathic medicine- liquid dilution-Pyrogenium200CH; Batch no: 0227513)
- And the temperature of all the fever induced rats were recorded one hourly with lubricated thermometer rectally to note the changes in the temperature.
- General blood parameters were checked before and after the administration of drug.
- The blood samples were collected before the administration of the drug and at 24 and 48 hours to analyze the blood parameters such as total WBC, neutrophils, eosinophil, lymphocytes, and platelets to know the prognosis.

4.6 OUTCOME ASSESSMENT

Temperature of all the animals of the three groups were recorded, and the group treated with Pyrogenium 200th potency is compared with the group treated with the paracetamol and the untreated group to assess the effectiveness of the homoeopathic medicine Pyrogenium 200 in reducing fever and the accessory symptoms produced in the experimental albino rats which is induced by Baker's yeast. And the blood parameters such as total WBC, neutrophils, lymphocytes, platelets, eosinophil were analyzed to know the prognosis before and after the administration of the drug.

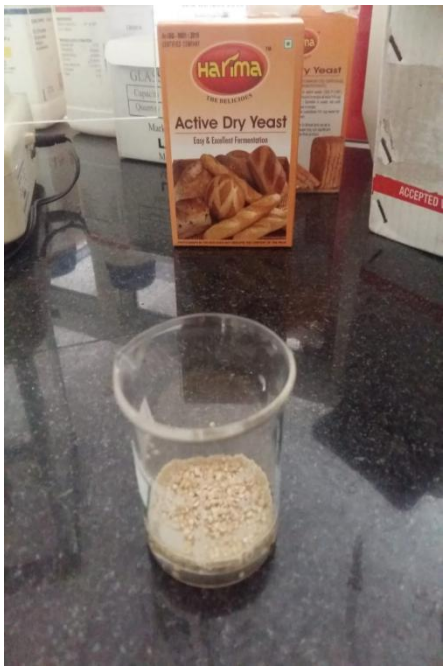
4.7 GIVING IDENTIFICATION MARK TO RAT



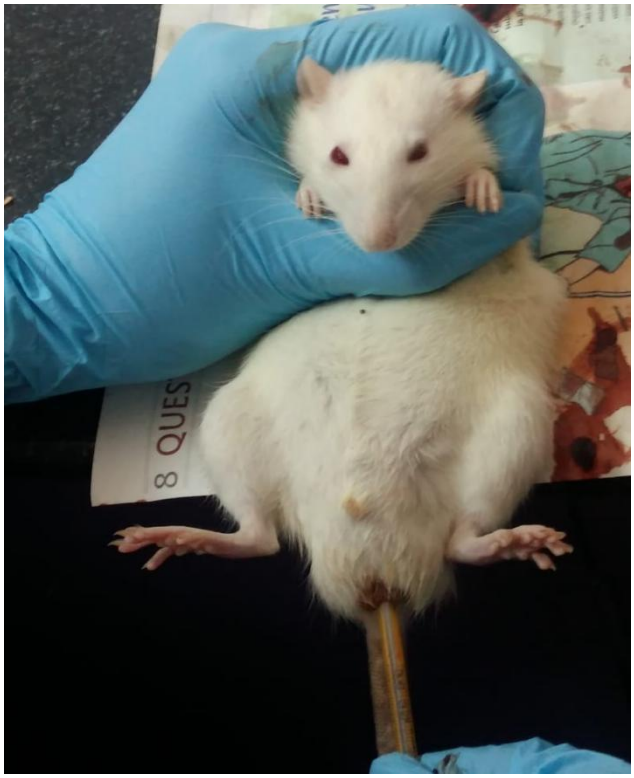
4.8 RATS IN CAGE WITH FOOD PELLETS AND WATER

4.9 WEIGHING THE RATS

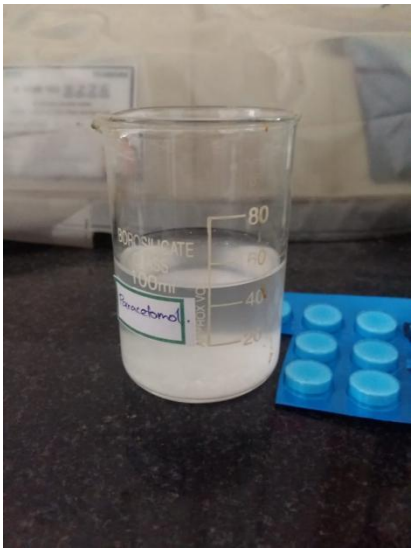
4.10 INJECTING BAKER'S YEAST INTRAPERITONEALLY



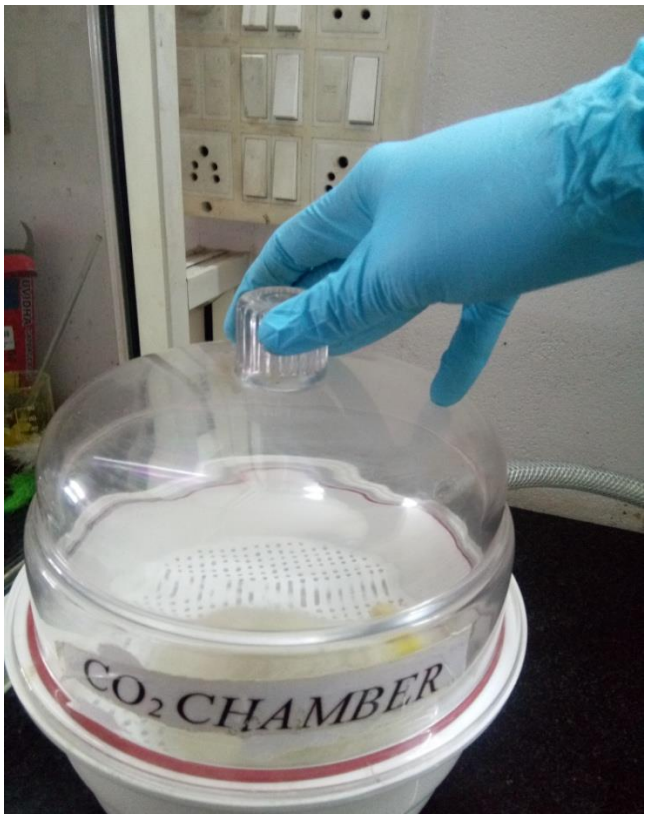
4.11 RECORDING THE TEMPERATURE



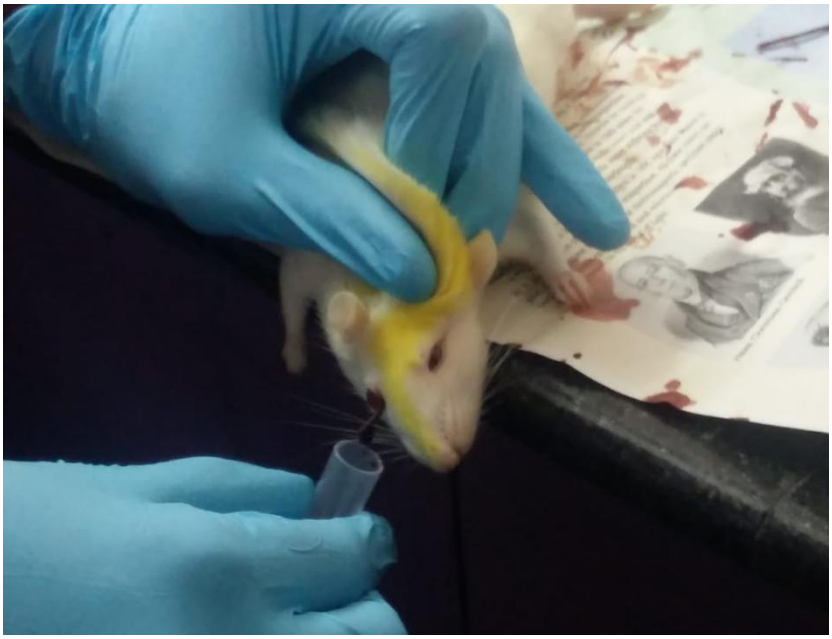
4.12 ADMINISTERING MEDICINE



4.13GIVING ANAESTHESIA TO THE RATS



4.12DRAWING BLOOD SAMPLE



5. OBSERVATIONS AND RESULTS

TABLE NO: 1

MEAN TEMPERATURE OF GROUP1-TREATED WITH SALINE

SL.NO	HOURS OF THE TEMPERATURE READING	MEAN TEMPERATURE OF GROUP 1
1	Intial temperature (before yeast induction)	98.433
2	Before intervention	101.2365
3	1st hour (after intervention)	103.5064
4	2nd hour	102.5999
5	3rd hour	102.3566
6	4th hour	102.3594
7	5th hour	100.8322
8	6th hour	101.2279
9	7th hour	101.3307
10	8th hour	101.5651
11	16th hour	101.5645
12	20th hour	101.1658
13	24th hour	101.1566

CHART NO: 1

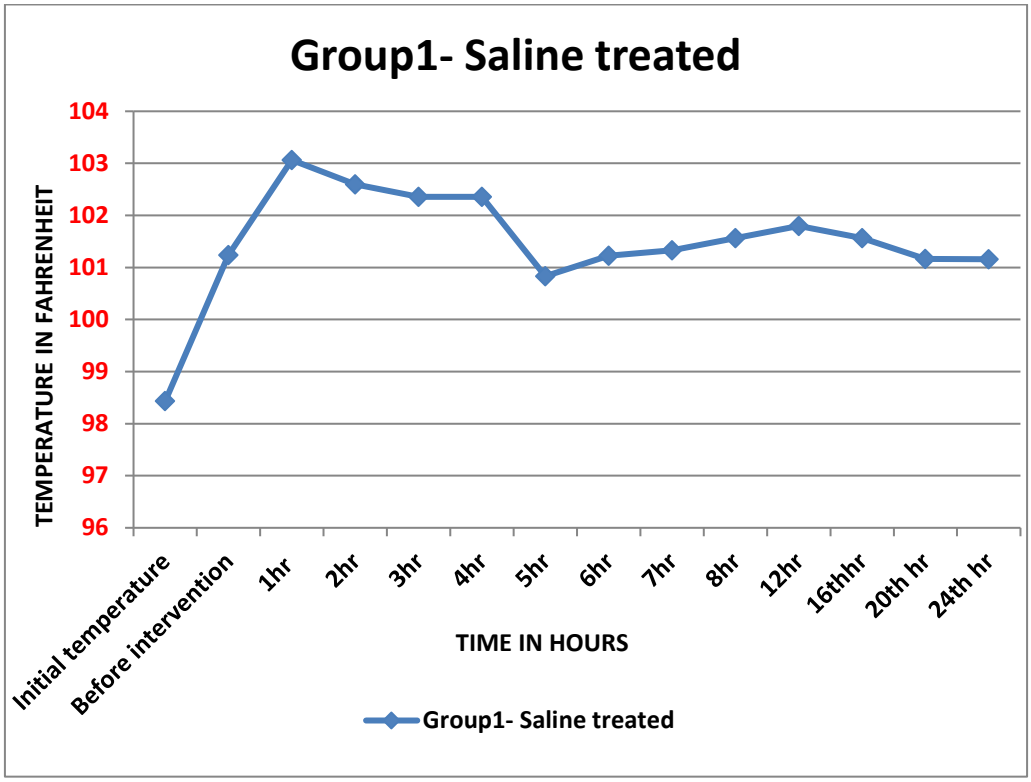

Group1- Saline treated
104
103
102
101
100
99
98
97
96
TEMPERATURE IN FAHRENHEIT
Initial temperature
Before intervention
1hr
2hr
3hr
4hr
5hr
6hr
7hr
8hr
12hr
16thhr
20th hr
24th hr
TIME IN HOURS
Group1- Saline treated

TABLE NO:2

MEAN TEMPERATURE OF GROUP 2-TREATED WITH PARACETOMOL

SL.NO	HOURS OF THE TEMPERATURE READING	MEAN TEMPERATURE OF GROUP 2
1	Intial temperature (before yeast induction)	97.633
2	Before intervention	101.1964
3	1st hour (after intervention)	99.931
4	2nd hour	101.0979
5	3rd hour	103.0299
6	4th hour	101.6323
7	5th hour	98.995
8	6th hour	100.7275
9	7th hour	100.7657
10	8th hour	100.4992
11	16th hour	100.6994
12	20th hour	100.5639
13	24th hour	100.3264

CHART NO:2

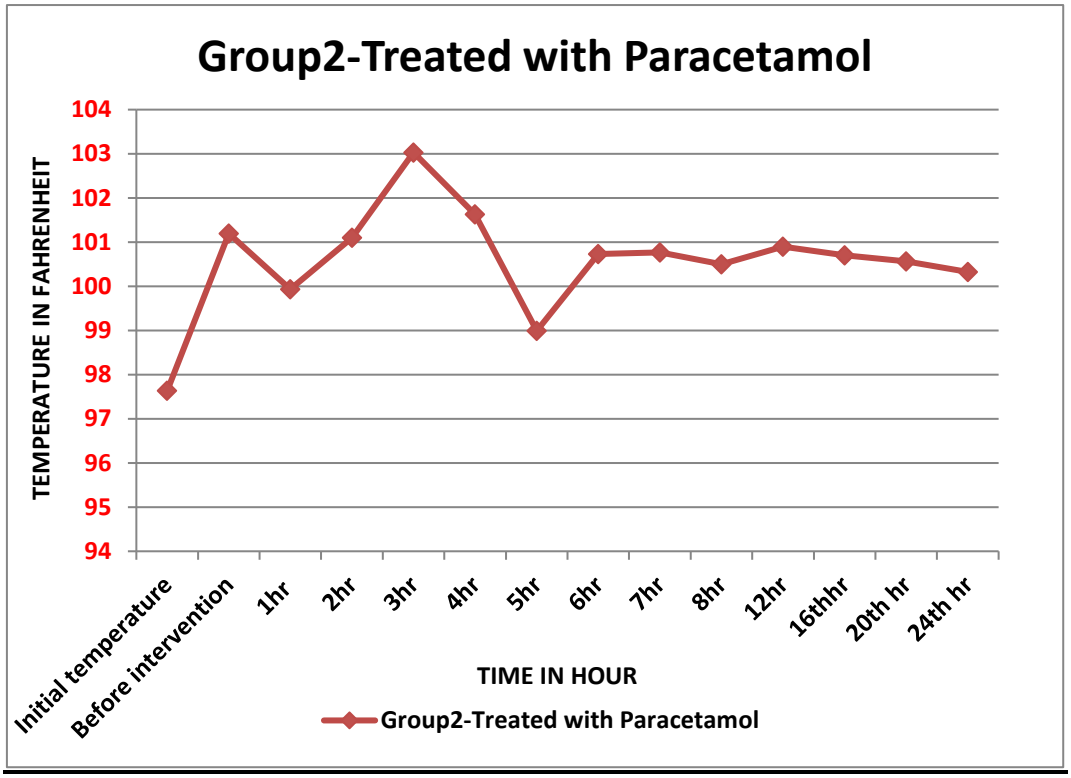

Group2-Treated with Paracetamol
TEMPERATURE IN FAHRENHEIT
104
103
102
101
100
99
98
97
96
95
94
Initial temperature
Before intervention
1hr
2hr
3hr
4hr
5hr
6hr
7hr
8hr
12hr
16thhr
20th hr
24th hr
TIME IN HOUR
Group2-Treated with Paracetamol

TABLE NO: 3

MEAN TEMPERATURE OFGROUP 3-TREATED

WITH PYROGENIUM 200

SL.NO	HOURS OF THE TEMPERATURE READING	MEAN TEMPERATURE OF GROUP 3
1	Intial temperature (before yeast induction)	97.633
2	Before intervention	101.6323
3	1st hour (after intervention)	102.5261
4	2nd hour	100.1947
5	3rd hour	100.6641
6	4th hour	99.9986
7	5th hour	98.96395
8	6th hour	98.63209
9	7th hour	99.2308
10	8th hour	99.09948
11	16th hour	99.13295
12	20th hour	98.93315
13	24th hour	98.93268

CHART NO: 3

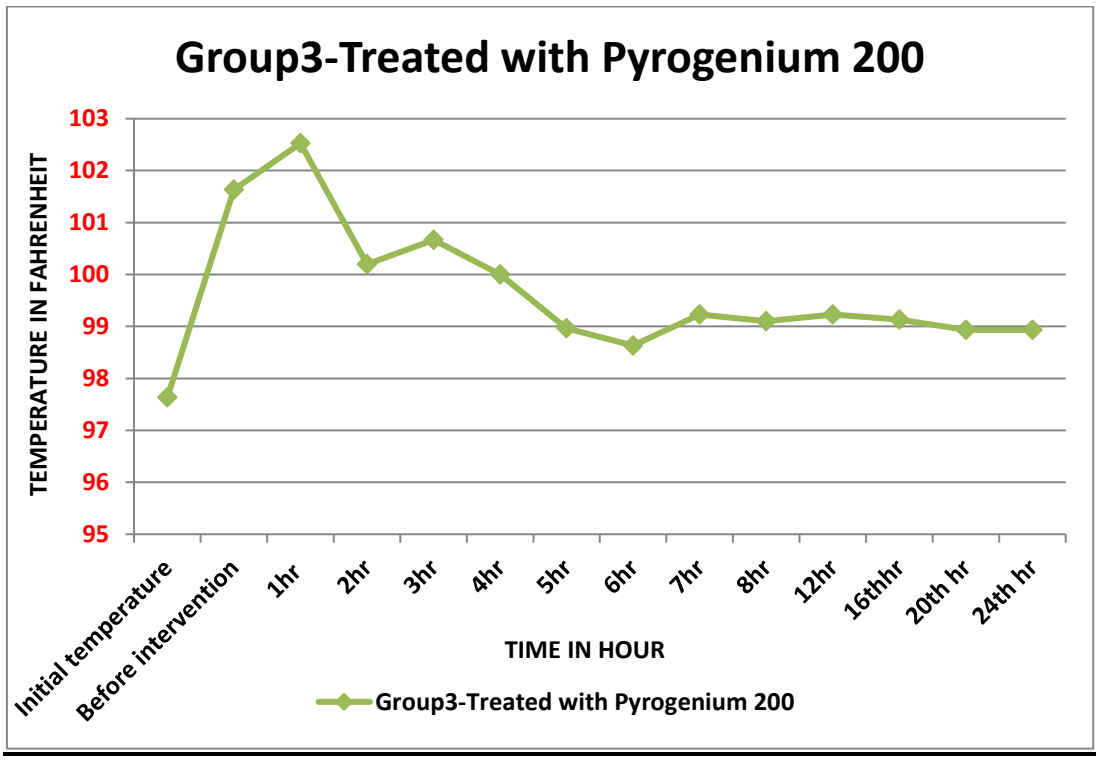

Group3-Treated with Pyrogenium 200
TEMPERATURE IN FAHRENHEIT
103
102
101
100
99
98
97
96
95
Initial temperature
Before intervention
1hr
2hr
3hr
4hr
5hr
6hr
7hr
8hr
12hr
16thhr
20th hr
24th hr
TIME IN HOUR
Group3-Treated with Pyrogenium 200

TABLE NO: 4

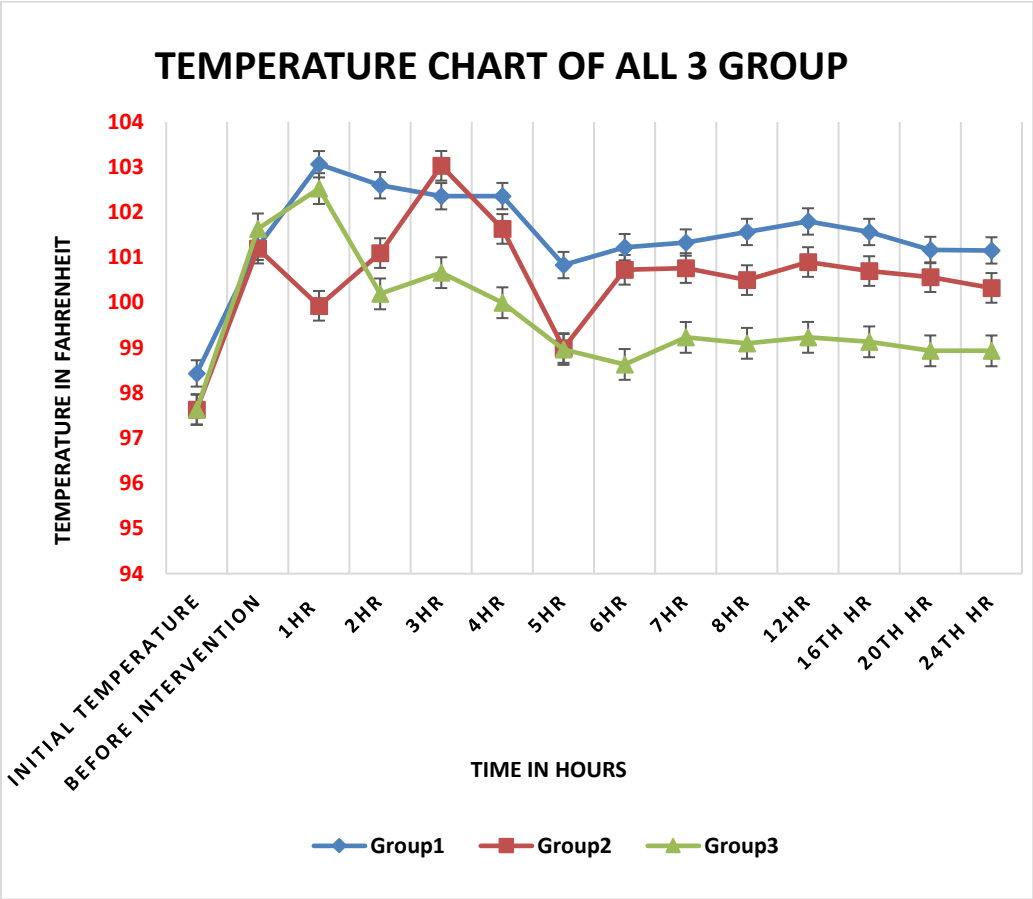
MEAN TEMPERATURE OF 3GROUP

SL.NO	HOURS OF THE TEMPERATURE READING	MEAN TEMPERATURE		
		GROUP 1	GROUP 2	GROUP 3
1	Initial temperature (Before yeast induction)	98.433	97.633	97.633
2	Before intervention	101.2365	101.1964	101.6323
3	1st hour (after intervention)	103.5064	99.931	102.5261
4	2nd hour	102.5999	101.0979	100.1947
5	3rd hour	102.3566	103.0299	100.6641
6	4th hour	102.3594	101.6323	99.9986
7	5th hour	100.8322	98.995	98.96395
8	6th hour	101.2279	100.7275	98.63209
9	7th hour	101.3307	100.7657	99.2308
10	8th hour	101.5651	100.4992	99.09948
11	16th hour	101.5645	100.6994	99.13295
12	20th hour	101.1658	100.5639	98.93315
13	24th hour	101.1566	100.3264	98.93268

***Initial temperature was noted before fever induction and hourly temperature was noted 4 hours after yeast induction and after the administration of drug.**

***Group 1 treated with saline; Group 2 treated with Paracetomol; Group 3 treated with Pyrogenium 200.**

CHART NO: 4



*Group 1 treated with saline;Group 2 treated with Paracetomol;Group 3 treated with Pyrogenium 200

TABLE NO: 5

MEAN VALUE OF BLOOD PARAMETERS

BEFORE YEAST INDUCTION

S.NO	GROUP	TC	PLATLETS	N	L	E
1	GROUP1	6416.66	683.3	27.83	66.5	3.8
2	GROUP2	6866.66	725	29.83	68.833	2.16
3	GROUP3	6766.66	733.33	30.33	68.16	2

CHART NO: 5

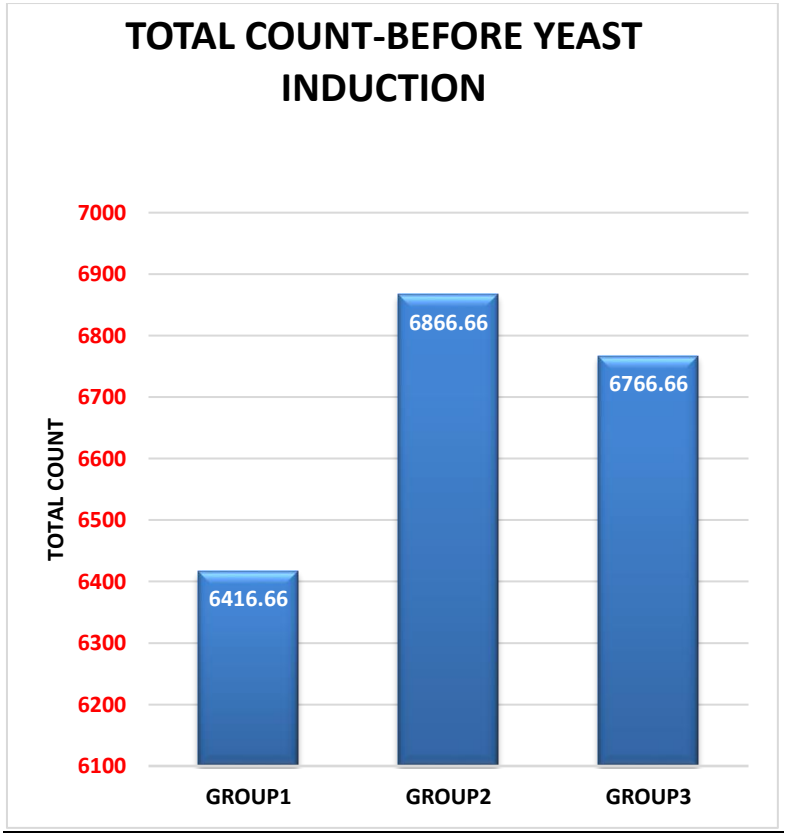


CHART NO: 6

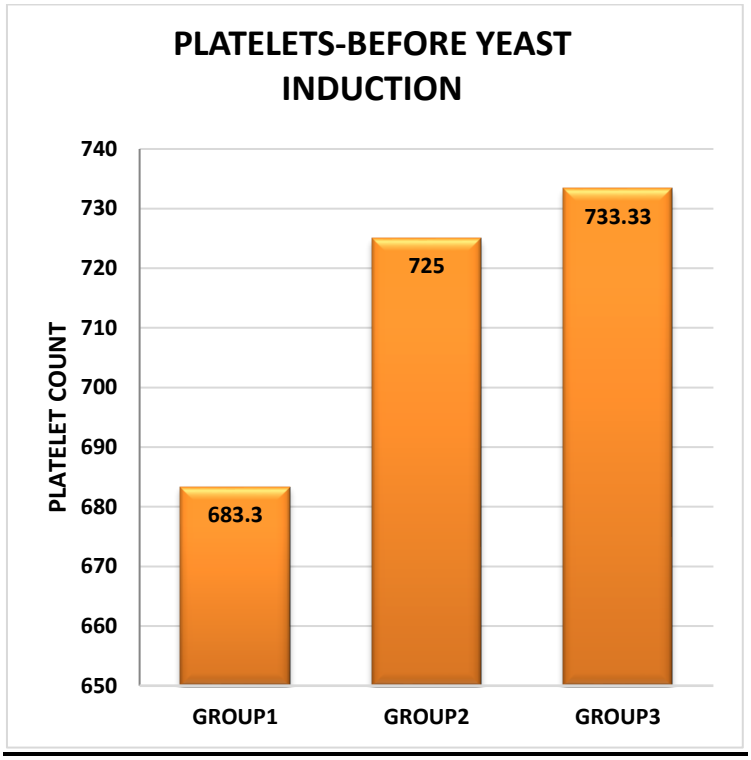


CHART NO: 7

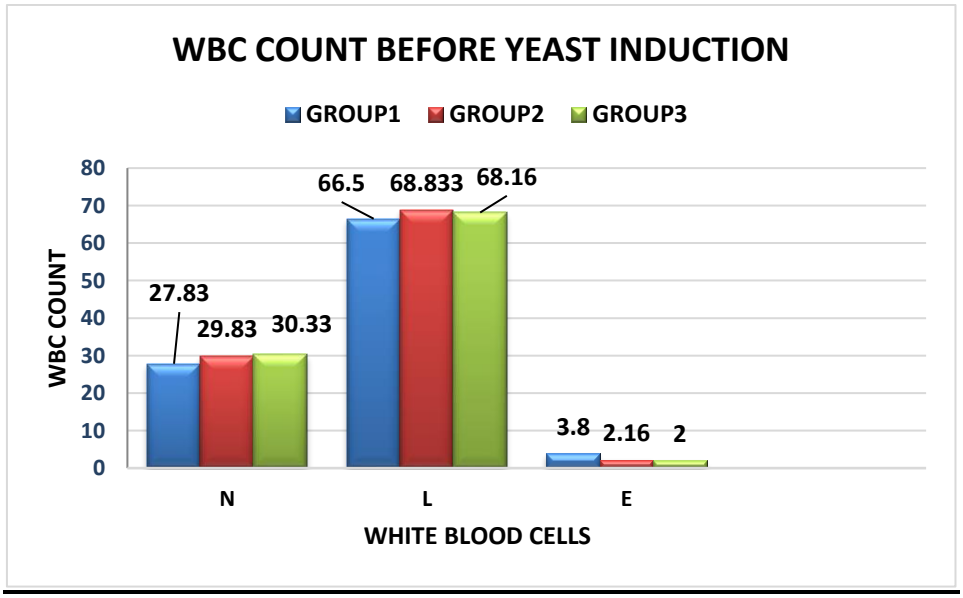


TABLE NO: 6

MEAN VALUE OF BLOOD PARAMETERS

AFTER YEAST INDUCTION

S.NO	GROUP	TC	PLATLETS	N	L	E
1	GROUP1	6366.66	620.833	26	62	3.833
2	GROUP2	6100	641.66	24.166	63.33	3
3	GROUP3	6400	616.66	26.33	63.5	3.16

CHART NO: 8

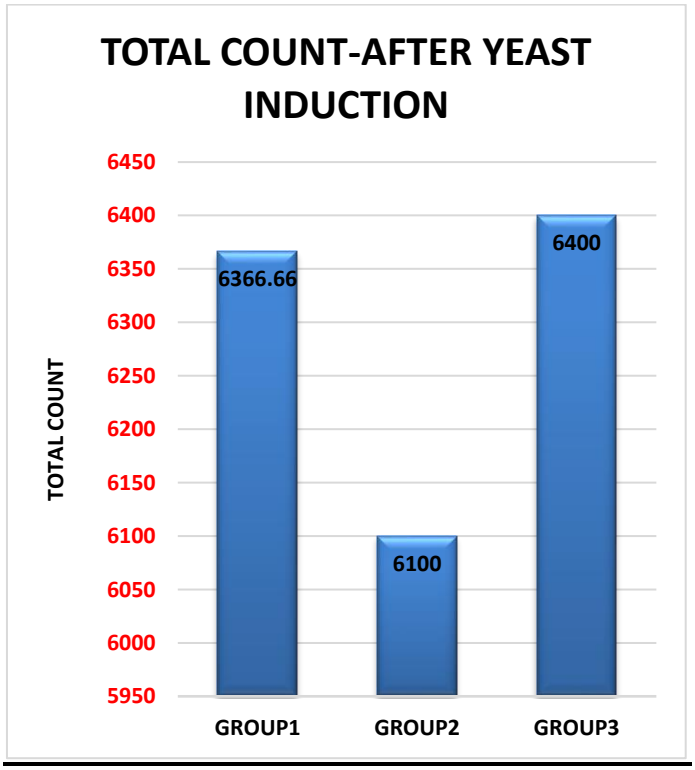


CHART NO:9

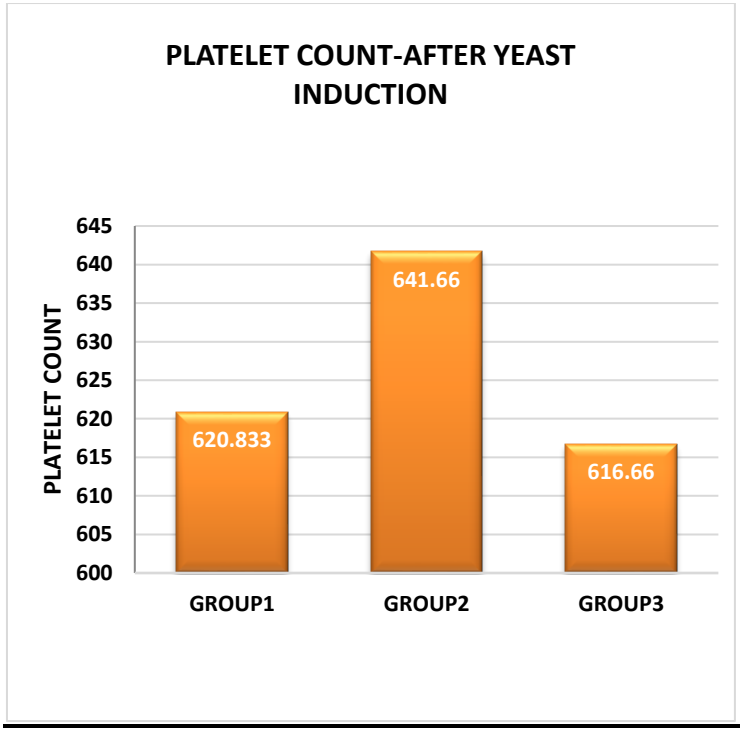


CHART NO:10

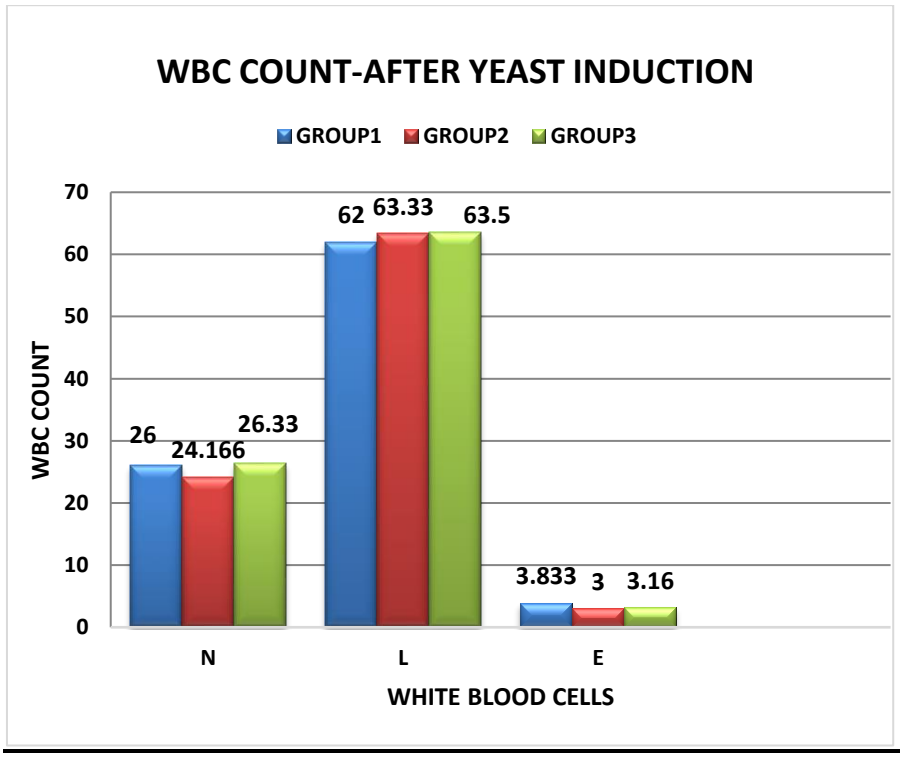


TABLE NO: 7

MEAN VALUE OF BLOOD PARAMETERS AFTER INTERVENTION

S.NO	GROUP	TC	PLATLETS	N	L	E
1	GROUP1	6816.66	620.83	26	62	3
2	GROUP2	6583.33	641.66	24.16	61.66	2.16
3	GROUP3	6866.667	641.66	32	69.166	1

CHART NO: 11

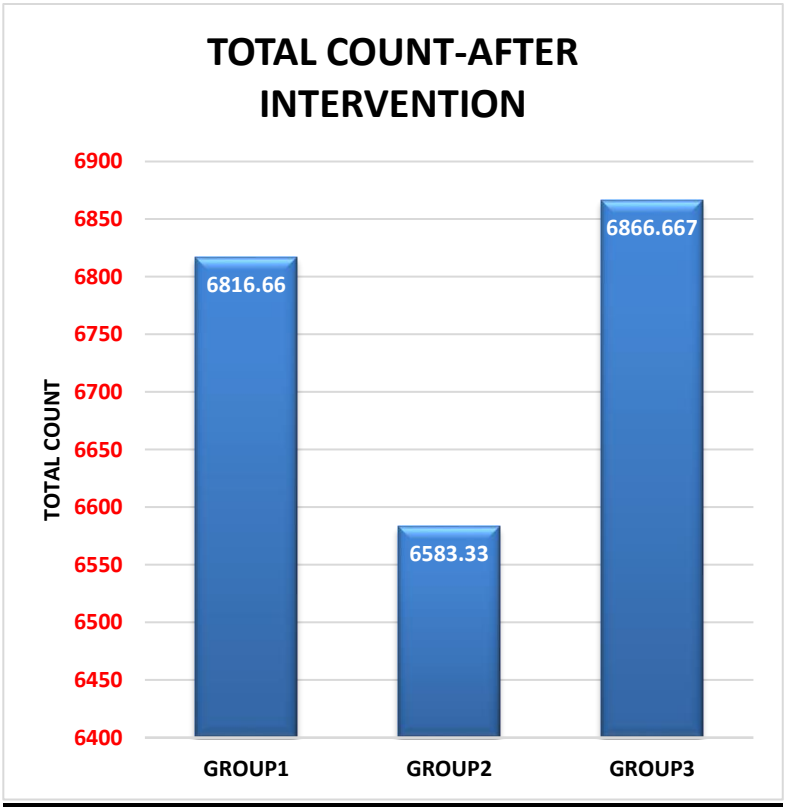


CHART NO: 12

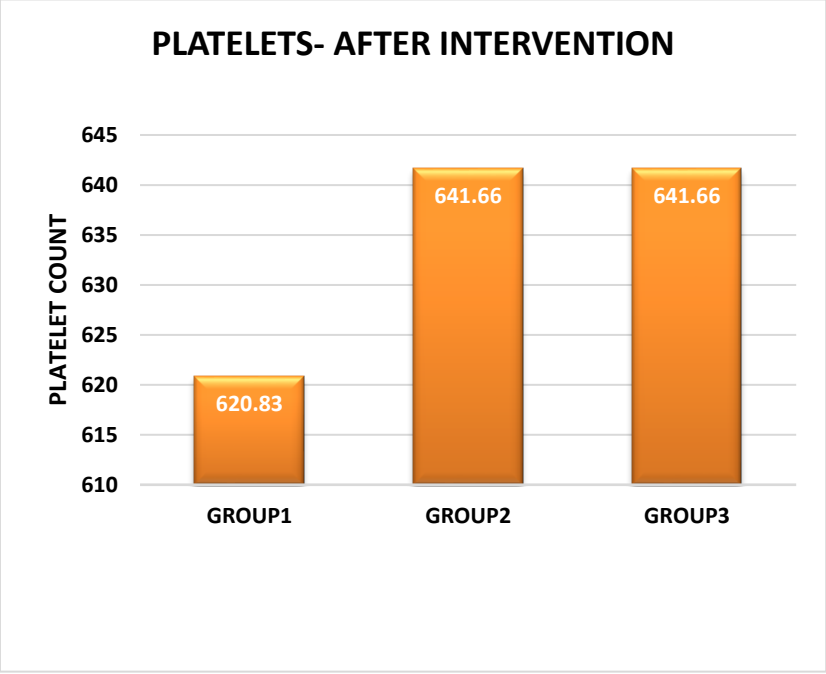


CHART NO: 13

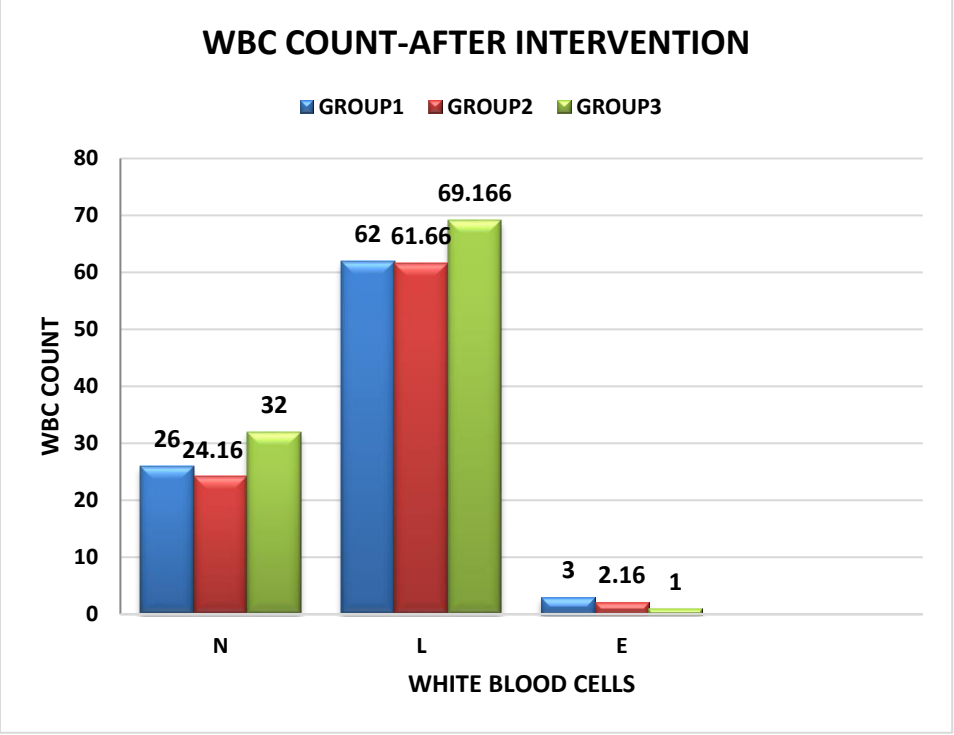


TABLE NO: 8

MEAN VALUE OF BLOOD PARAMETERS OF 3 GROUP

BLOOD PARAMETERS	BEFORE YEAST INDUCTION			AFTER YEAST INDUCTION			AFTER INTERVENTION		
	G1	G2	G3	G1	G2	G3	G1	G2	G3
TOTAL COUNT	6416.6	6866.66	6766.66	6366.66	6100	6400	6816.66	6583.33	6866.667
PLATELETS	683.3	725	733.33	620.833	641.66	616.66	620.83	641.66	641.66
NEUTROPHIL	27.83	29.83	30.33	26	24.166	26.33	26	24.16	32
LYMPHOCYTE	66.5	68.833	68.16	62	63.33	63.5	62	61.66	69.166
EOSINOPHIL	3.8	2.16	2	3.833	3	3.16	3	2.16	1

CHART NO: 14

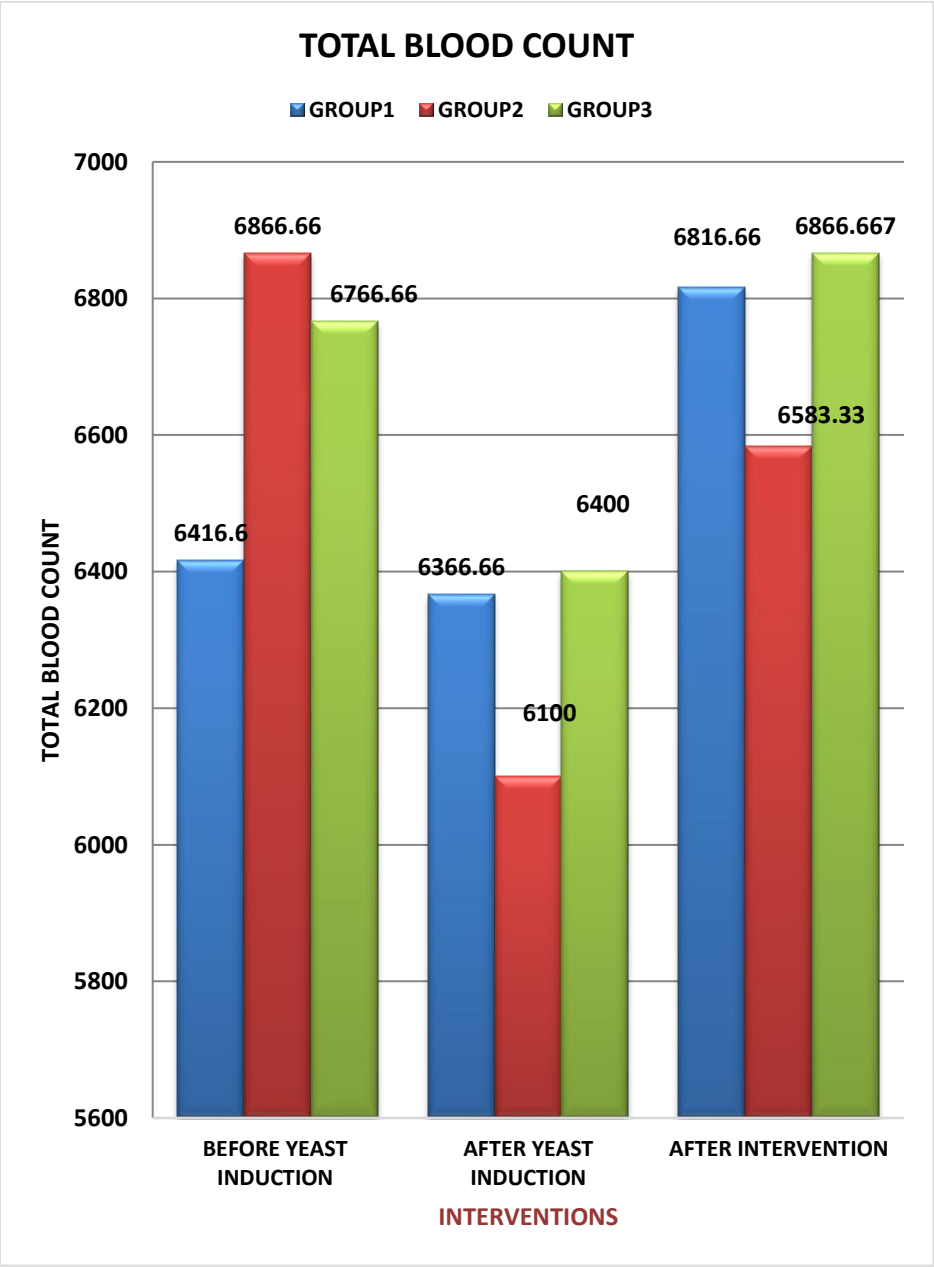

TOTAL BLOOD COUNT
GROUP1
GROUP2
GROUP3
7000
6800
6600
6400
6200
6000
5800
5600
TOTAL BLOOD COUNT
6866.66
6766.66
6816.66
6866.667
6583.33
6400
6416.6
6366.66
6100
BEFORE YEAST INDUCTION
AFTER YEAST INDUCTION
AFTER INTERVENTION
INTERVENTIONS

CHART NO: 15

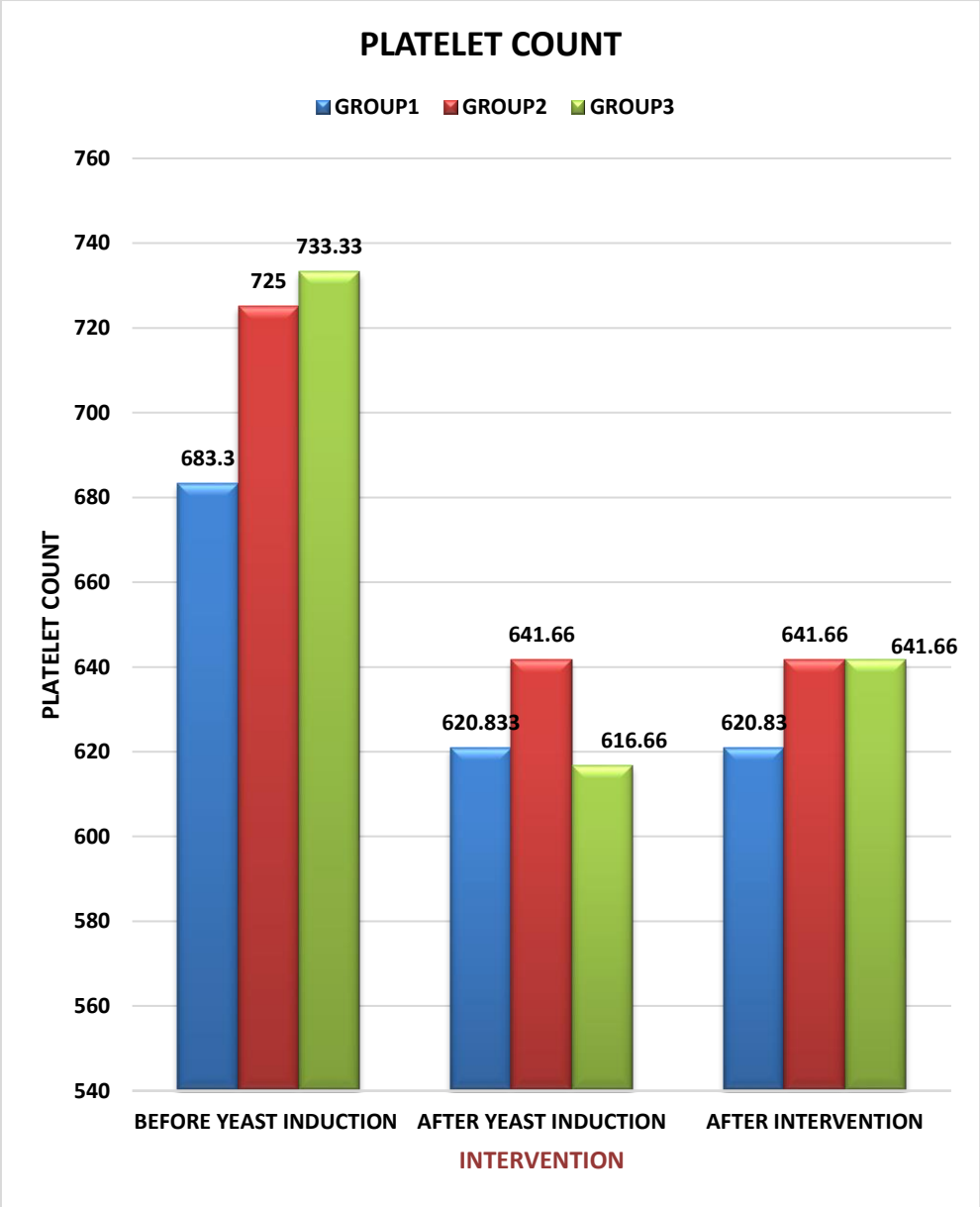

PLATELET COUNT
GROUP1
GROUP2
GROUP3
760
740
720
700
680
660
640
620
600
580
560
540
PLATELET COUNT
683.3
725
733.33
620.833
641.66
616.66
620.83
641.66
641.66
BEFORE YEAST INDUCTION
AFTER YEAST INDUCTION
AFTER INTERVENTION
INTERVENTION

CHART NO: 16

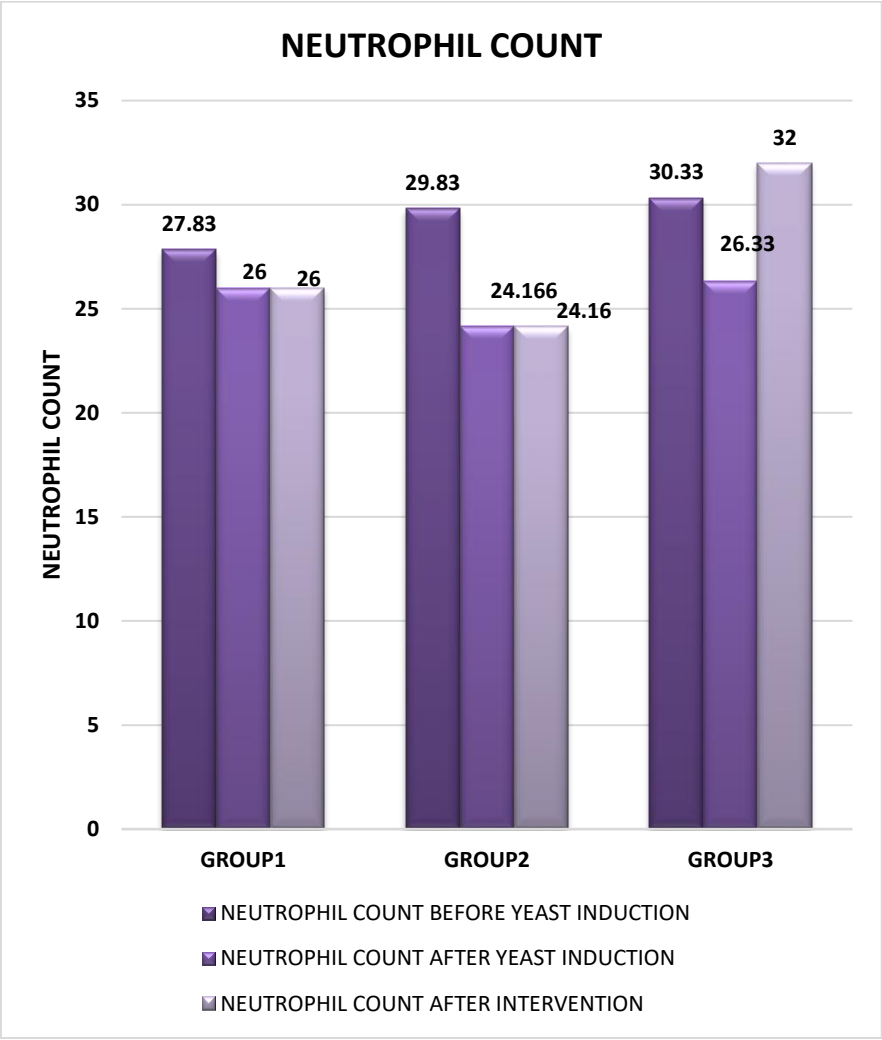

NEUTROPHIL COUNT
35
30
25
20
15
10
5
0
NEUTROPHIL COUNT
27.83
26
26
29.83
24.166
24.16
30.33
26.33
32
GROUP1
GROUP2
GROUP3
NEUTROPHIL COUNT BEFORE YEAST INDUCTION
NEUTROPHIL COUNT AFTER YEAST INDUCTION
NEUTROPHIL COUNT AFTER INTERVENTION

CHART NO: 17

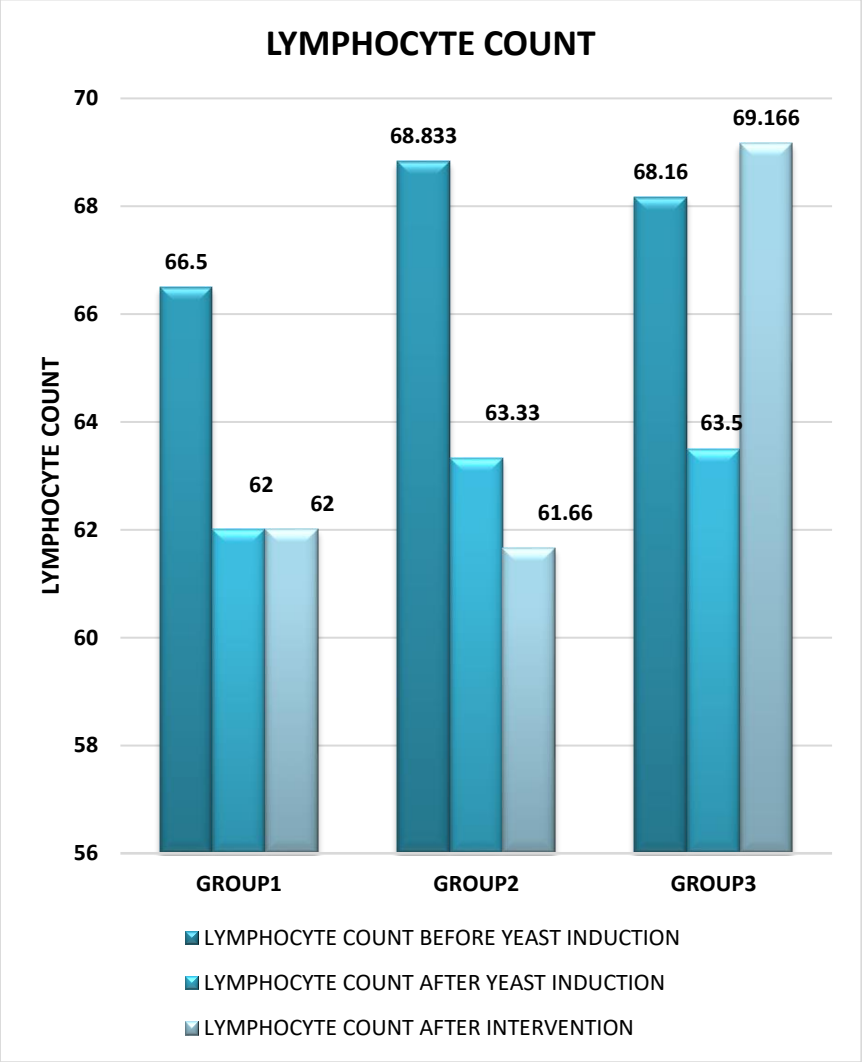
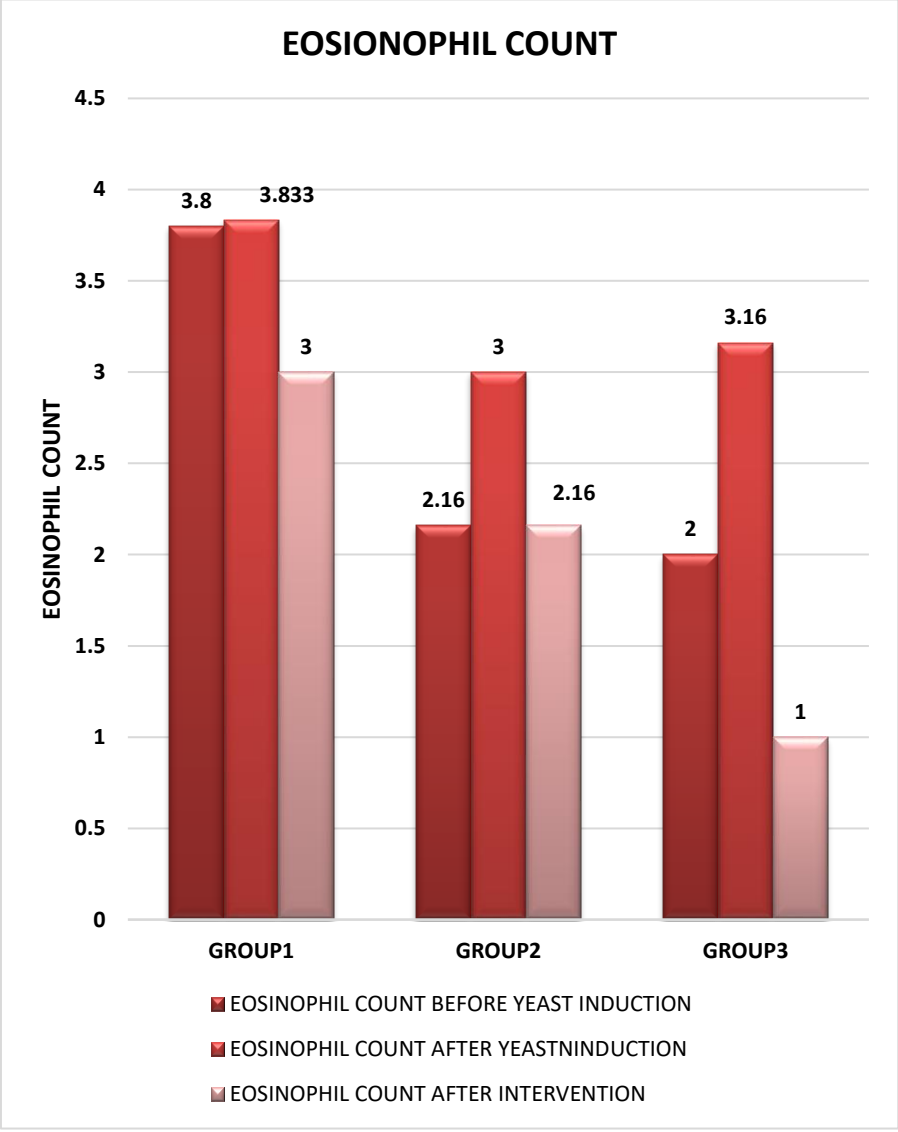

LYMPHOCYTE COUNT
LYMPHOCYTE COUNT
70
68
66
64
62
60
58
56
66.5
62
62
68.833
63.33
61.66
68.16
63.5
69.166
GROUP1
GROUP2
GROUP3
LYMPHOCYTE COUNT BEFORE YEAST INDUCTION
LYMPHOCYTE COUNT AFTER YEAST INDUCTION
LYMPHOCYTE COUNT AFTER INTERVENTION

CHART NO:18


EOSIONOPHIL COUNT
EOSINOPHIL COUNT
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
3.8
3.833
3
2.16
3
2.16
2
3.16
1
GROUP1
GROUP2
GROUP3
EOSINOPHIL COUNT BEFORE YEAST INDUCTION
EOSINOPHIL COUNT AFTER YEASTNINDUCTION
EOSINOPHIL COUNT AFTER INTERVENTION

5.1 OBSERVATION AND RESULTS:

Before baker's yeast induction normal temperature was noted in all the animals in 3 group. And fever developed after 4hours of baker's yeast induction in all rats and then the intervention was made according to the group. After intervention the temperature was recorded 1hourly until the temperature comes to normal range. The intervention was made at the interval of 4hours.

After intervention it is observed that group 1 which is treated with saline the temperature shoots up to 103°F in the 1st hour from 101.2°F before intervention, then it starts reducing to102°F and sustained up to 4th hour. At 5th hour it reduced to 100°F. From 6th to 20th hour the temperature remained at 101°F then it reduced to 100.6°F at 24th hour.

In group 2 it is observed that after administration of standard medicine paracetamol at the 1st hour the temperature was reduced to 99.9°F from 101.1°F before intervention, then it increased to101°F ,103°F at 2nd and 3rd hour respectively. At the 5th hour it reduced to 98.9°F which it reached to the normal range when the intervention was repeated after 4th hour. Then the temperature shoots up to 100°F at 6th hour and it sustained up to 24th hour.

It is observed in group3 which is treated with Pyrogenium 200 shows a homoeopathic aggravation by raise of temperature from 101.6°F to 102.5°F at the 1st hour after intervention and then it started to reduce to100°F at the 3rd hour and to 99°F at the 4th hour. At the 6th hour the temperature was at 98.6°F. From 7th hour to 16th hour the temperature sustained at 99°F and decreased to 98.9°F.

It is observed that compared with the untreated group and group treated with Paracetamol, Pyrogenium 200 has reduced fever at the 2nd hour after the intervention.

Whereas in untreated group the fever remained till 24th hour and in group treated with Paracetamol, it is noted that the temperature lowered only at after intervention.

Blood samples taken from orbital sinus of all samples before Baker's yeast induction, after yeast induction and 48 hours after intervention to evaluate the changes in the blood parameters such as total blood count, platelets, neutrophils, lymphocytes and eosinophils.

All the parameters were in normal range in the samples which collected before Baker's yeast induction.

It is found that after Baker's yeast induction all the level of blood parameter reduced slightly in all 3 groups.

When compared the level of blood parameters after intervention with the level of after baker's yeast induction, there was a rise in total blood count in 3 groups. The platelet count and neutrophil count was at the same level in untreated group and in group treated with Paracetamol, but in group treated with Pyrogenium 200 shows elevation in platelet and neutrophil count.

The lymphocyte and eosinophil count in untreated group was remained same as before but it reduced slightly in group treated with Paracetamol.

In group treated with Pyrogenium 200 the lymphocyte count was raised and the eosinophil count got reduced.

6. STATISTICAL ANALYSIS

6.1 ANALYSIS OF VARIANCE OF TEMPERATURE

TABLE NO:9

SOURCE	GROUP- 1	GROUP -2	GROUP-3	Total
N	13	13	13	39
∑X	1319.3346	1307.0976	1295.5739	3922.0061
Mean	101.4873	100.546	99.6595	100.564
$\sum X^2$	133912.6441	131442.8974	129137.2835	394492.825
Std.Dev.	1.1891	1.2748	1.3228	1.4436

Source	***SS***	***df***	***MS***	
Between-treatments	21.7208	2	10.8604	***F* = 6.80344**
Within-treatments	57.4671	36	1.5963	
Total	79.1879	38		

Inference:

The f-ratio value is 6.80344. The p-value is .003117. The result is significant at p < .05.

Post Hoc Tukey HSD (beta)

Pairwise Comparisons		$HSD_{.05}$ = 1.2113 $HSD_{.01}$ = 1.5405	$Q_{.05}$ = 3.4568 $Q_{.01}$ = 4.3961
G_1:G_2	M_1 = 101.49 M_2 = 100.55	0.94	Q = 2.69 (*p* = .15346)
G_1:G_3	M_1 = 101.49 M_3 = 99.66	1.83	**Q = 5.22** (*p* = .00209)
G_2:G_3	M_2 = 100.55 M_3 = 99.66	0.89	Q = 2.53 (*p* = .18767)

6.2 ANALYSIS OF VARIANCE OF BLOOD PARAMETERS

TABLE NO:10

10.1 TOTAL BLOOD COUNT

Source	DF	Sum of Square (SS)	Mean Square (MS)	F Statistic (df_1,df_2)	P-value
Interventions	2	378563.4172	189281.7086	4.6052 (2,4)	**0.09168**
Groups	2	47105.4765	23552.7382	0.573 (2,4)	**0.6042**
Error	4	164407.3778	41101.8445		
Total	**8**	**590076.2715**	**73759.5339**		

10.2 PLATELET COUNT

Source	DF	Sum of Square (SS)	Mean Square (MS)	F Statistic (df_1, df_2)	P-value
Interventions	2	13990.6418	6995.3209	35.5079 (2,4)	***0.002843***
Groups	2	1297.0483	648.5241	3.2919 (2,4)	**0.1428**
Error	4	788.0302	197.0076		
Total	**8**	**16075.7203**	**2009.465**		

10.3 NEUTROPHIL COUNT

Source	DF	Sum of Square (SS)	Mean Square (MS)	F Statistic (df_1,df_2)	P-value
Interventions	2	22.0202	11.0101	2.3676 (2,4)	**0.2097**
Groups	2	21.2339	10.617	2.283 (2,4)	**0.2181**
Error	4	18.6016	4.6504		
Total	**8**	**61.8557**	**7.732**		

10.4 LYMPHOCYTE COUNT

Source	DF	Sum of Square (SS)	Mean Square (MS)	F Statistic (df_1, df_2)	P-value
Interventions	2	38.3063	19.1531	3.5394 (2,4)	**0.1304**
Groups	2	18.5234	9.2617	1.7115 (2,4)	**0.2904**
Error	4	21.6454	5.4114		
Total	**8**	**78.4751**	**9.8094**		

10.5 EOSINOPHIL COUNT

Source	DF	Sum of Square (SS)	Mean Square (MS)	F Statistic (df_1, df_2)	P-value
Interventions	2	2.4517	1.2258	6.1231 (2,4)	**0.06062**
Groups	2	3.5921	1.7961	8.9714 (2,4)	**0.03323**
Error	4	0.8008	0.2002		
Total	**8**	**6.8446**	**0.8556**		

6.3 INTERPRETATION OF STATISTICAL RESULT

Compared to untreated group homoeopathic medicine Pyrogenium 200 has showed significant results with p value less than 0.05. There was a specific reduction in temperature in the group treated with Paracetamol but the temperature was remained at the normal range till the end in the group treated with Pyrogenium 200 after a homoeopathic aggravation at the first hour of after administration of the remedy.

The total blood count among intervention since p-value > α, H0 cannot be rejected. The p-value equals **0.09168**, (p (x≤4.6052) = 0.9083). The test statistic **FA** equals **4.6052**, which is in the 95% region of acceptance: [-∞: 6.9443]. The p value is not statistically significant. Among group since p-value > α, H0 cannot be rejected. The p-value equals **0.6042**, (p(x≤0.573) = 0.3958. The test statistic **FA** equals **0.573**, which is in the 95% region of acceptance: [∞:6.9443]. The p value is not statistically significant.

The platelet count among intervention, since p-value < α, H0 is rejected. The p-value equals **0.002843**, (p (x≤35.5079) = 0.9972. The test statistic **FA** equals **35.5079**, which is not in the 95% region of acceptance: [-∞: 6.9443]. The p value is statistically significant. Among group since p-value > α, H0 cannot be rejected. The p-value equals **0.1428**, (p (x≤3.2919) = 0.8572). The p value is not statistically significant. The test statistic **FA** equals **3.2919**, which is in the 95% region of acceptance: [-∞: 6.9443].

The neutrophil count among intervention, since p-value > α, H0 cannot be rejected.The p-value equals **0.2097**, (p(x≤2.3676) = 0.7903). The test statistic **FA** equals **2.3676**, which is in the 95% region of acceptance: [-∞: 6.9443]. Among group since p-value > α, H0 cannot be rejected. The p-value equals **0.2181**, (p (x≤2.283) =

0.7819). The larger the p-value the more it supports H0. The p value is not statistically significant. The test statistic **FA** equals **2.283**, which is in the 95% region of acceptance: [-∞: 6.9443].

The lymphocyte count among intervention since p-value > α, H0 cannot be rejected. The p-value equals **0.1304**, (p (x≤3.5394) = 0.8696). The p value is not statistically significant. The test statistic **FA** equals **3.5394**, which is in the 95% region of acceptance: [-∞: 6.9443]. Among group since p-value > α, H0 cannot be rejected. The p-value equals **0.2904**, (p (x≤1.7115) = 0.7096). The p value is not statistically significant. The test statistic **FA** equals **1.7115**, which is in the 95% region of acceptance: [-∞: 6.9443].

The eosinophil count among intervention, since p-value > α, H0 cannot be rejected. The p-value equals **0.06062**, (p (x≤6.1231) = 0.9394. The p value is not statistically significant. The test statistic **FA** equals **6.1231**, which is in the 95% region of acceptance: [-∞: 6.9443]. Among group since p-value < α, H0 is rejected. The p-value equals **0.03323**, (p (x≤8.9714) = 0.9668). The p value is statistically significant. The test statistic **FA** equals **8.9714**, which is not in the 95% region of acceptance: [-∞: 6.9443].

7. DISCUSSION

Fever which means a body temperature above the usual range of normal can be caused by abnormalities in the brain itself or by toxic substances that affect the temperature regulating centers.

The experiment setup was made in cape Bio research Lab, Marthandam. 18 wistar albino rats were divided in o 3 groups and group 1 is treated with saline which is considered as untreated group, group2 is tread with Paracetamol and group 3 is treated with homoeopathic medicine Pyrogenium 200. Baker's yeast is used to induce fever in animals and the temperature is noted rectally by lubricated thermometer for every 1 hour and intervention was made 4 hourly.

From the study it is found that in the untreated group where saline was given as the intervention showed no improvement in the temperature and in the blood parameters.

In the group treated with Paracetamol the temperature reduced after intervention then it increased and when the intervention is repeated again after 4hours the temperature falls down again.

In group 3 which is treated with homoeopathic medicine Pyrogenium 200 a homoeopathic aggravation was noted as a rise of temperature in an hour after intervention. Which proves the Kent's third observation the is "*Aggravation is Quick, Short and Strong with Rapid Improvement of the Patient* "[32].Where he says this is the classical homoeopathic aggravation and it is usually seen in few hours after administering the remedy. This could be observed in the condition when the administered remedy is a similimum. When such a similimum is administered, at times a temporary intensification of the symptoms may occur. This aggravation shall

be mild and usually last only for a short period after the administration of the medicine. The homeopathic medicinepossesses dynamic properties where other school of medicine contain pharmacologically active ingredients. The dynamic effect of thehomeopathic medicine is the one that acts on the subject.[33]

The homeopathic aggravation after the administration of the curative remedy is the reaction of the organism, as it responds to the gently stimulating action of the medicine. This aggravation may only be a slight intensification of symptoms and may hardly be noticed. [33][34]

As Hahnemann said in aphorism 158 of Organon of Medicine, a slight homoeopathic aggravation in the first hours is a good indication that the acute disease will probably be cured. If aggravation is marked, or if it persists, this may because the patient is proving the remedy, because a remedy that is poorly matched may actually induce new symptoms in the patient.[33][34]

According to aphorism 157 "An appropriately chosen homoeopathic remedy gently removes the disease without producing any new symptoms. It is, nevertheless, usual in the first few hours if the dose is too large (too low a potency) for it to effect some small aggravation". From aphorism 161 and 247 it is said that aggravations do not occur if the accurately chosen homoeopathic medicine is given in low potencies which are gradually increased and modified by higher potencies.[33][34]

From these, it is evident that homoeopathic aggravations are a part of homoeopathic treatment, as such concept do not exist in other medical system.[33][34]

The temperature in the group 3 comes to the normal range faster than when compared with the untreated group and the group treated with the Paracetamol.

When compared the level of blood parameters after intervention with the level of after baker's yeast induction, there was a rise in total blood count in 3 groups. The platelet count and neutrophil count was at the same level in untreated group and in group treated with Paracetamol, but in group treated with Pyrogenium 200 shows elevation in platelet and neutrophil count. The lymphocyte and eosinophil count in untreated group was remained same as before but it reduced slightly in group treated with Paracetamol. In group treated with Pyrogenium 200 the lymphocyte count was raised and the eosinophil count got reduced.

With the blood parameters it is observed that the group treated with Pyrogenium 200 showed better immunogenic response when compared with the untreated group and the group treated with the Paracetamol.

8. CONCLUSION

Pyrogenium 200 is more effective in treating pyrexia in Baker's yeast induced fever in wistar albino rat models.

Pyrogenium 200 is effective in reducing the temperature efficiently when comparing with untreated rats and the rats treated with Paracetamol without any recurrence of rise of temperature except homoeopathic aggravation. Thus Pyrogenium 200 possesses a marked antipyretic activity.

Homoeopathic medicine Pyrogenium 200 can produce a better immunogenic response than the untreated rats and rats treated with Paracetamol, thus it is increasing the immunity which leads to improvement.

From this it is evident that homoeopathic aggravations are a part of homoeopathic treatment, as such concept do not exist in other medical system.

The p value is than 0.05 for the parameters such as temperature, platelets indicating that the test is significant. For total blood count, neutrophils, eosinophil the p value is greater than 0.05 indicating that it is due to chance.

9.SUMMARY

Pyrexia was induced to a sample size of 18 wistar albino rats (divided randomly into 3groups containing 6 animals each) Baker's yeast induction through intraperitoneally after 1 week of acclimatization. After induction of fever all the animals received their respective treatment at an interval of 4 hours and the temperature was recorded 1 hourly. The blood samples were collected before and after Baker's yeast induction and also 48 hours after treatment for the analysis of blood parameters.

It was found that the group treated with homoeopathic medicine Pyrogenium 200 showed better result than other group 1 and group 2, in immunogenic response and in reducing fever, from the 2^{nd} hour of intervention which followed after a homoeopathic aggravation at the 1^{st} hour and then it reduced and sustained within the normal range. Whereas when compared with the group treated with standard medicine Paracetamol, the temperature reduced only whenever the interventions are made and it did not sustained within the normal range. In untreated group there was no reduction in temperature.

10.LIMITATIONS

- Individualization is not done in this study.
- Competence of homoeopath to do an experimental study.
- Acceptance by homoeopaths for an experimental study.
- Challenging the concept of disease which is dynamic in origin.
- Visible changes could not be noted in blood parameters, whereas longer time duration would be helpful in understanding the variables among the group, which is identified as limitation of this study.

10.1RECOMMENDATIONS

- Studies using animal models of different pathology and different medicine can be done.
- The same study can be done using different medicine.
- Bigger sample size with extended time of research would provide better results especially in blood parameters.

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