

PHARMACOLOGICAL SCREENING COMBINATION OF PARACETAMOL AND SUCROSE

Sandhya sree.M*, B.Rohitreddy, A.Mary Navaneetha, CH. Mounika, A.Rajashekar
Reddy, Karthik.M, A Salomy Monica Diyya, J.Gautami.

*Assistant Professor, Department of pharmacology, Bharat Institute of Technology,
Ibrahimpattam,India, 501510.

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*Correspondence for

Author

Sandhya Sree.M

Assistant Professor,
Department of pharmacology,
Bharat Institute of Technology,
Ibrahimpattam,India, 501510.

ABSTRACT

Analgesic drugs act in various ways on the peripheral and central nervous systems. Pharmacological screening combination of Paracetamol and sucrose on mice and rats using Tail immersion method, Carrageenan induced rat paw edema method and Antipyretic activity was performed. Test group with paracetmol + sucrose 35% showed maximum analgesic and anti-inflammatory activity with the use of tail immersion and carrageenan method. Prostaglandin analogue like Misoprostol in tail immersion method, the analgesic response was reduced when compared with standard& test groups without prostaglandin analogues. The paracetmol coated with sucrose can be formulated which decreases the rejection of paracetmol for its bitter taste.

KEY WORDS: Analgesic, sweet, prostaglandin.

INTRODUCTION

An analgesic, or painkiller, is any member of the group of drugs used to achieve analgesia — relief from pain. Previous studies report that the ingestion of highly concentrated sweet solutions produces a morphine-like analgesia in rats, human infants, and in adult males. To determine whether sweet-induced analgesia occurs with more commonly consumed substances, 30 adult males (Mage = 22.4 years) were exposed to a cold pressor test and pain responsivity was assessed both before and after consuming either an 8% sucrose solution, water, or nothing. Between-groups comparisons revealed that relative to the Sucrose or Nothing groups, the Water group showed increased pain tolerance. Neither pain thresholds nor ratings of pain intensity and unpleasantness on a visual analogue scale differed among

groups. The results support previous findings in both humans and animals that the palatability or hedonic value of food or drink may be the key predictor of its analgesic effect. The efficacy of paracetamol when used in combination with weak opioids (such as codeine) was assessed in data studies in 1996 and 2009, which found improved efficacy for approximately 50% of patients but increases in the number of patients experiencing adverse effects. Combination drugs of paracetamol and strong opioids like morphine reduce the amount of opioid needed and improve analgesic effect.

Animal profile: Animal: Albino mice and Wistar rats, Gender: Male, Body weight: Mice— (35g-40g) of 2 months old, Rats --- (250g-300g) of 1 year old

Dose calculations

150 mg/Kg body weight of paracetamol was administered in a constant volume of 0.2 ml using oral Gavage. Standard drug (S) of 150 mg/Kg body weight of paracetamol suspended in water and administered in a constant volume of 0.2ml.

Test drug preparations

Paracetamol 150mg/kg body weight and sucrose 35% combination (T1) was prepared

Paracetamol 150mg/kg body weight and sucrose 30% combination (t1) was prepared

S.No	control	Test (t1)	Test (T1)	Standard (S)
Number of animals	3	3	3	3
Dose	0.2ml	0.2ml	0.2ml	0.2ml
Drug	Water	Paracetamol 150mg/kg + sucrose 30%	Paracetamol 150mg/kg + sucrose 35%	Paracetamol 150mg/kg

Screening method: 1. tail immersion method

1. Weight the animals and number them
2. Each rat is kept in individual cylindrical rat holders such that the tail hangs freely
3. Mark the tail at 5cm from tip. Immersed in hot water (55°C)
4. Animal immediately withdraws its tails and the time taken is recorded by using stopwatch
5. The test substance administered.
6. Note the reaction time 0,30,60,90,120min
7. 2. carrageenin induced rat paw edema method
8. Weight the animal and number them

9. Make a mark on both hind paws (right & left)so that every time the paw is dipped in the mercury column up to the fixed mark to ensure constant paw volume
10. Note the individual paw volume (both right & left)of each rat by mercury displacement method
11. Divided the animals in four groups it should be at least three rats in one group inject the Test drug (35% sucrose+150mg/kg paracetamol)
12. Noted readings before carrageen & after carrageen
13. Thirty minutes later the rats are challenged by S.C injection of 0.05 ml of 1% solution of carrageenin on the plantar surface of left hind paw.
14. Note the reaction time 0th min, 1hr, 2hr
15. 3. antipyretic activity
16. In rats subcutaneous injection of brewer's yeast suspension produces significant pyrexia which can be counteracted by clinically effective antipyretic drugs.

METHODS

Wistar rats are divided in groups of three animals each. Their initial temperature is recorded by insertion of a thermo couple to a depth of 2cm into the rectum..A 15% suspension brewer's yeast in 0.9% saline is injected subcutaneously in back below the nape of the neck in a dose of 10 ml/kg. The site of injection is massaged in order to spread the suspension beneath the skin. The room temperature is maintained between 22-24^oc immediately of the yeast injection the food is withdrawn and at 18h post challenge the rise in rectal temperature is recorded the observation is repeated after 30min. Only animals with a body temperature of at least 38^oc are included in this test. These animals received the test compounds or standard drug by oral administration and their rectal temperature are recorded at 30,60,120,180min thereafter. The maximum reduction in average rectal temperature in comparison with the control hyperpyrexia group is calculated and the results are compared with the effect of a standard drug like paracetamol

TABLES AND GRAPHS

Table 1: Tail immersion method

Test:- 35% sucrose+ 150MG/kg of paracetamol ;test:- 30% sucrose+ 150mg/KG paracetamol;

Standard:- 150mg/KG of paracetamol; Control:- water

Treatment groups	Mean reaction time				
	0 th min	30 th min	60 th min	90 th min	120 th min
Test(T)	2sec	5.6sec	4.6sec	5sec	4.6sec
test(t)	1.3sec	3.3sec	4.45sec	4.3sec	4.3sec
Standard	1sec	2.3sec	3sec	3.6sec	4.2sec
Control	1.6sec	2.3sec	2.6sec	2.3sec	2.3sec

TABLE 2: Carrageenan induced rat paw edema method

s.no	Treatment groups		Mean paw volume in ml		
			0 th min	1hr	2hr
1	Control	c	0.3	0.29	0.26
2	Standard	s	0.29	0.17	0.14
3	Test	T	0.3	0.15	0.14
4	Test	t	0.3	0.17	0.14

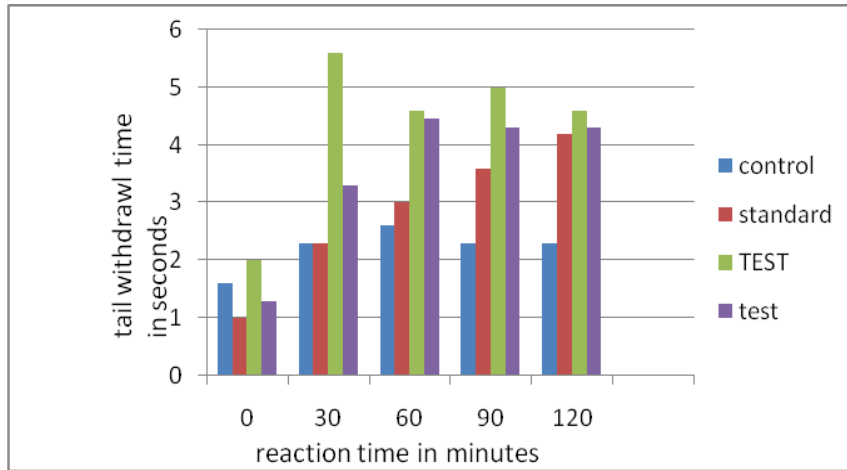
TABLE 3: Antipyretic activity

S.NO	Treatment groups	Before yeast injection (temperature °c)	After yeast injection (temperature °c)				
			0	30	60	120	180
1	C	35	40	39	38	38	38
2	S	34	39	38	36	34	34
3	T	35	40	38	36	35	34
4	t	34	40	38	37	33	33

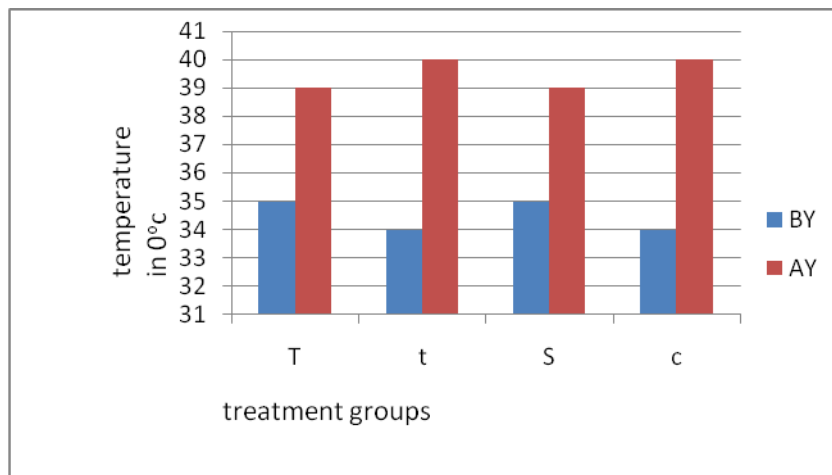
TABLE 4: Effect of prostaglandin analogues on paracetamol and paracetamol+sucrose combination using tail immersion method.

Groups	Dose of drug	Time(sec)			
		0	30	60	90
C ₁	Misoprostal	3	3	2	2
C ₂	Water	3	3	3	3
T	Paracetamol+sucrose(35%)+M	4	4	3	2
t	Paracetamol+sucrose(30%)+M	4	4	3	3
S	Paracetamol+M	4	5	4	4

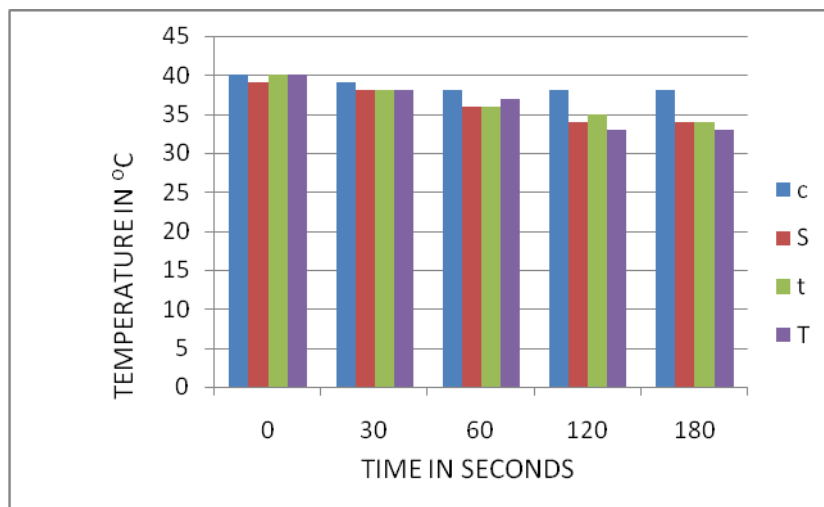
M-Misoprostil



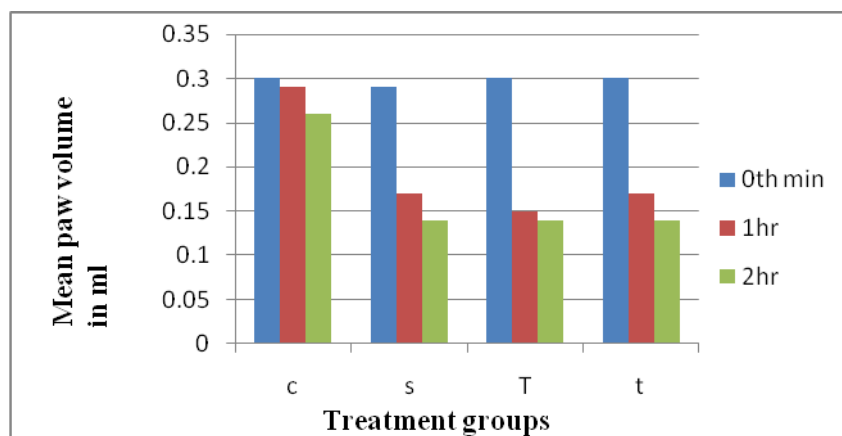
GRAPH-1 Tail immersion method



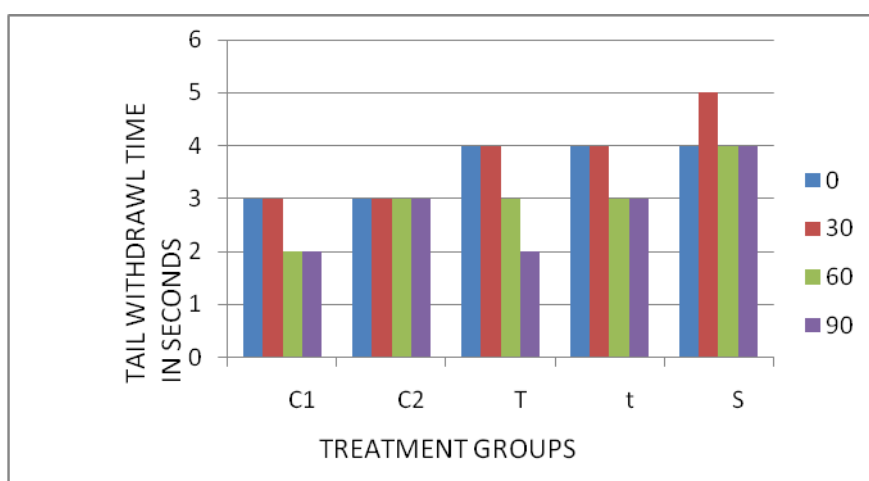
GRAPH-2 Antipyretic activity



GRAPH-3



GRAPH-4 Carrageenan induced rat paw edema method



GRAPH-5. Effect of prostaglandin analogues on paracetmol and paracetmol+sucrose combination using tail immersion method.

CONCLUSION

Maximum analgesic response at 60 min in case of T and t for standard drug at 120min. Maximum analgesic response with Test(T) when compared to t & S. Maximum reduction in 2hrs and sudden reduction from 0.3 to 0.15. Test(T) has shown more reduction in paw edema when compared with test(t) and standard(S). Reduction in temperature with S, T & t was observed. Test group (t) maximum reduced temperature at 120°C. Almost all groups have shown similar reduction in temperature. With prostaglandin analogue like Misoprostol in tail immersion method. The analgesic response was reduced when compared with standard & yeast groups without prostaglandin analogues. The above results indicate prostaglandins presence is suppressing the analgesic response of standard and test drugs. The underlying mechanism under the synergistic effect

can be through this inhibition of prostaglandin levels further studies on with different screening methods and with opioid antagonists can be performed.

It is concluded that the test group with paracetmol + sucrose 35% showed maximum analgesic and anti-inflammatory activity with the use of tail immersion and carrageenan method.

The combination on further screening on different analgesic, anti-inflammatory and antipyretic methods is encouraged to further analyse the combinational effect of paracetmol and sucrose from the above results the paracetmol coated with sucrose can be formulated which decreases the rejection of paracetmol for its bitter taste. It is also concluded from the above results that this sucrose coated paracetmol not only improves palatability of bitter drug paracetmol but also improves pharmacological activity of paracetmol. It is also concluded from the results that prostaglandin level reduction mechanism underlying pharmacological activity of combinational drugs.

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