PHARMACOLOGICAL SCREENING COMBINATION OF PARACETAMOL AND SUCROSE


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

Test drug preparations
Paracetmol 150mg/kg body weight and sucrose 35% combination (T1) was prepared
Paracetmol 150mg/kg body weight and sucrose 30% combination (t1) was prepared

<table>
<thead>
<tr>
<th>S.No</th>
<th>control</th>
<th>Test (t1)</th>
<th>Test (T1)</th>
<th>Standard (S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of animals</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Dose</td>
<td>0.2ml</td>
<td>0.2ml</td>
<td>0.2ml</td>
<td>0.2ml</td>
</tr>
<tr>
<td>Drug</td>
<td>Water</td>
<td>Paracetmol150mg/kg+sucrose 30%</td>
<td>Paracetmol150mg/kg+sucrose 35%</td>
<td>Paracetmol150mg/kg</td>
</tr>
</tbody>
</table>

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 paracetmol)

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 of 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 inorder to spread the suspension beneath the skin. The room temperature is maintain between 22-24°C 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°C are included in this test. This 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 hyperpyrexic 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 paracetmol; Standard: - 150mg/KG of paracetmol; Control: - water
### Table 1: Mean reaction time

<table>
<thead>
<tr>
<th>Treatment groups</th>
<th>0&lt;sup&gt;th&lt;/sup&gt; min</th>
<th>30&lt;sup&gt;th&lt;/sup&gt; min</th>
<th>60&lt;sup&gt;th&lt;/sup&gt; min</th>
<th>90&lt;sup&gt;th&lt;/sup&gt; min</th>
<th>120&lt;sup&gt;th&lt;/sup&gt; min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test(T)</td>
<td>2sec</td>
<td>5.6sec</td>
<td>4.6sec</td>
<td>5sec</td>
<td>4.6sec</td>
</tr>
<tr>
<td>test(t)</td>
<td>1.3sec</td>
<td>3.3sec</td>
<td>4.45sec</td>
<td>4.3sec</td>
<td>4.3sec</td>
</tr>
<tr>
<td>Standard</td>
<td>1sec</td>
<td>2.3sec</td>
<td>3sec</td>
<td>3.6sec</td>
<td>4.2sec</td>
</tr>
<tr>
<td>Control</td>
<td>1.6sec</td>
<td>2.3sec</td>
<td>2.6sec</td>
<td>2.3sec</td>
<td>2.3sec</td>
</tr>
</tbody>
</table>

### Table 2: Carrageenan induced rat paw edema method

<table>
<thead>
<tr>
<th>s.no</th>
<th>Treatment groups</th>
<th>Mean paw volume in ml</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>0&lt;sup&gt;th&lt;/sup&gt; min</td>
</tr>
<tr>
<td>1</td>
<td>Control</td>
<td>c</td>
</tr>
<tr>
<td>2</td>
<td>Standard</td>
<td>s</td>
</tr>
<tr>
<td>3</td>
<td>Test</td>
<td>T</td>
</tr>
<tr>
<td>4</td>
<td>Test</td>
<td>t</td>
</tr>
</tbody>
</table>

### Table 3: Antipyretic activity

<table>
<thead>
<tr>
<th>S.NO</th>
<th>Treatment groups</th>
<th>Before yeast injection (temperature °C)</th>
<th>After yeast injection (temperature °C)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>30</td>
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<td>1</td>
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<td>35</td>
<td>40</td>
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<tr>
<td>2</td>
<td>S</td>
<td>34</td>
<td>39</td>
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<tr>
<td>3</td>
<td>T</td>
<td>35</td>
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</tr>
<tr>
<td>4</td>
<td>t</td>
<td>34</td>
<td>40</td>
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</table>

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

<table>
<thead>
<tr>
<th>Groups</th>
<th>Dose of drug</th>
<th>Time(sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>C&lt;sub&gt;1&lt;/sub&gt;</td>
<td>Misoprostal</td>
<td>3</td>
</tr>
<tr>
<td>C&lt;sub&gt;2&lt;/sub&gt;</td>
<td>Water</td>
<td>3</td>
</tr>
<tr>
<td>T</td>
<td>Paracetamol+sucrose(35%)+M</td>
<td>4</td>
</tr>
<tr>
<td>t</td>
<td>Paracetamol+sucrose(30%)+M</td>
<td>4</td>
</tr>
<tr>
<td>S</td>
<td>Paracetamol+M</td>
<td>4</td>
</tr>
</tbody>
</table>

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 0.3to 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 carrageenam 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.

REFERENCES

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