Antipruritic Effects of Yanggyeoksanhwa-tang (YGSHT) on Scratching Behavior induced by Compound 48/80 in Mice

Seungyeob Ryu
Dept. of Sasang Constitutional Medicine, College of Korean Medicine, Wonkwang University 460 Iksandae-ro, Iksan, Jeonbuk, Republic of Korea inside000@hanmail.net

Abstract. The purpose of this research is to investigate antipruritic effects of Yanggyeoksanhwa-tang (YGSHT) in herbal formula for Sasang constitutional medicine (four-constitution medicine). This study focuses on searching pharmacological activity of crude drugs in YGSHT prescription and evaluated effects of 70% EtOH extracts and fractions from YGSHT on scratching behavior induced by compound 48/80 in ICR mice. YGSHT extracts and fractions are dissolved in saline and administered orally as 12.5 mg/kg, 25 mg/kg, 50 mg/kg, and 100 mg/kg. YGSHT extracts (50 mg/kg) and EtOAc fractions (2.5 mg/kg) clearly reduce scratching responses elicited by compound 48/80 in mice. These results suggest that YGSHT widely affects pruritus, and is possible to be used as antipruritic agents.

Keywords: Yanggyeoksanhwa-tang (YGSHT), Sasang constitutional medicine, antipruritic

1 Introduction

Pruritus is an unpleasant sensation that urges people to scratch the skin. This symptom is commonly observed in skin disease and it has bad impact on the physical, mental and psychological well-being [1].

Sasang constitutional medicine is unique Korean traditional medicine; characters of human beings are classified into four types (Tae-Yang, So-Yang, Tae-Eum, and So-Eum) depending on one’s innate Nature and Emotion. Each type has own physiological, pathological, pharmacological, and dietary characteristics [2].

Yanggyeoksanhwa-tang (YGSHT) has been widely used in Sasang constitutional medicine for treatment of So-Yang symptomatology such as inflammation, diabetes, pain, stroke, skin diseases [3].

Therefore, this study focuses on revealing pharmacological activity of crude drugs in YGSHT prescription and evaluated the effects of 70% EtOH extracts and fractions from YGSHT on scratching behavior induced by compound 48/80 in ICR mice.
2 Materials and Methods

2.1 Animals

Animals used for this study are 5 week-old male ICR mice (Orient, Korea), weighing 20-25g and housed at 23 ± 2 °C, 55 ± 10 % and 12-h light/dark cycle (lighting time: 8:00-20:00) with food and water ad libitum.

2.2 YGSHT Extraction and Fractionation

Crude drug-composition according to YGSHT prescription is given in Table 1. YGSHT 70% EtOH extracted yield is 8.29%. Yields of fractionated EtOH extracts are EtOAc fractions (11.0%), n-BuOH fractions (8.9%), Hexane fractions (0.3%), and H2O fractions (41.3%), respectively.

<table>
<thead>
<tr>
<th>Korean name</th>
<th>Latin name</th>
<th>Dosage(g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ji Hwang</td>
<td>Rehmanniae Radix</td>
<td>8</td>
</tr>
<tr>
<td>In Dong</td>
<td>Lonicerae Folium et Caulis</td>
<td>8</td>
</tr>
<tr>
<td>Yeon Gyo</td>
<td>Forsythiae Fructus</td>
<td>8</td>
</tr>
<tr>
<td>Chi Ja</td>
<td>Gardeniae Fructus</td>
<td>4</td>
</tr>
<tr>
<td>Bak Ha</td>
<td>Menthae Herba</td>
<td>4</td>
</tr>
<tr>
<td>Ji Mo</td>
<td>Anemarrhenae Rhizoma</td>
<td>4</td>
</tr>
<tr>
<td>Seok Go</td>
<td>Gypsum</td>
<td>4</td>
</tr>
<tr>
<td>Hyeong Gae</td>
<td>Schizonepetae Spica</td>
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</tr>
<tr>
<td>Bang Pung</td>
<td>Saposhnikoviae Radix</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>48</strong></td>
</tr>
</tbody>
</table>

2.3 Induce and Measure Scratching Behavior

YGSHT extracts and fractions are dissolved in saline and administered orally as 12.5 mg/kg, 25 mg/kg, 50 mg/kg, and 100 mg/kg. After 1h, compound 48/80 (50mg/kg) is injected subcutaneously in both shoulders. Immediately after injection, scratching behavior is measured for 30min.

2.4 Statistical Analysis

Obtained results are expressed as a mean ± SEM. Statistical analyses are carried out using one-way ANOVA. Newman-Keuls test is used for comparisons after analysis of variance. Statistical significance is defined as $P < 0.05$. 
3 Results

3.1 Effect of YGSHT Extracts and Fractions

As shown in Fig. 1, YGSHT extracts effectively inhibit scratching behavior induced by compound 48/80 and effect is shown significant difference at all tested doses. Especially, it represents an excellent effect at doses of 50 mg/kg. YGSHT EtOAc fractions are significantly reduced a scratching behavior compared to the control group but significant difference is not found at n-BuOH, Hexane, and H2O fractions.

![Fig. 1. Effect of YGSHT extracts and fractions on scratching behavior induced by compound 48/80 (50µg/mouse, s.c.) in ICR mice. Each bar represents mean ± S.E.M of 8-10 mice. P values for group comparisons are obtained by one way ANOVA followed by Newman-Keuls test (*P < 0.05 as compared with control group).](image)

3.2 Effect of YGSHT EtOAc Fractions

![Fig. 2. Effect of YGSHT EtOAc fractions on scratching behavior induced by compound 48/80 (50µg/mouse, s.c.) in ICR mice. Each bar represents mean ± S.E.M of 8-10 mice. P values for group comparisons are obtained by one way ANOVA followed by Newman-Keuls test (*P < 0.05 as compared with control group).](image)
According to results of YGSHT fractions, effect of YGSHT EtOAc fractions (0.6, 1.2, and 2.5 mg/kg) is investigated on compound 48/80-induced scratching behavior (Fig. 2).

As shown in Fig. 2, YGSHT EtOAc fractions are significantly reduced the number of scratching behavior at the tested dose of 2.5 mg/kg.

4 Discussion

In this study, scratching behavior is induced by compound 48/80. It can cause histamine release from human mast cells, rats, and mice [4]. Histamine is well known to be present in mast cells and has been thought to be an important mediator of pruritus [5]. Recent research studies show that crude drugs in YGSHT prescription exert antipruritic, analgesic, immunomodulatory, and anti-inflammatory effects [6].

This study demonstrates that YGSHT extracts and fractions affect scratching behavior induced by compound 48/80. YGSHT extracts have an excellent effect at the tested dose of 50 mg/kg and EtOAc fractions out of fractions of YGSHT are shown a positive effect. YGSHT EtOAc fractions have a significant effect at the tested dose of 2.5 mg/kg.

In conclusion, results are showing that YGSHT extracts and EtOAc fractions are bioactive composite compounds having antipruritic effects.

References


* Due to the space limitation, result has been selected and reorganized to a presentable form.