The Effect Of Combination Of Curcuma Xanthorrhiza Roxb. Extract And Andrographis Paniculata Ness. Extract On Human Gallbladder

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ABSTRACT
Active compounds found in Curcuma xanthorrhiza dan Andrographis paniculata have the cholekinetic effect. The aim of the present study is to compare the cholekinetic effect produced by single dose of C.xanthorrhiza extract and A.paniculata extract administered separately or in combine on healthy adult volunteers (4 males ; 2 females, age: 20-30 years old and body weight 48.5-63 kg). The Gallbladder Contraction (GBC) for each treatment were increase with the time and significantly different for all comparison either based on time (p < 0.01) or treatment (p < 0.05) at 1 and 1.5 hours after taking the medicine. The percentage of GBC at 2 h after administration of 20 mg A. paniculata (74,58± 8,27%) or 40 mg C. xanthorrhiza extract (71,93±13,43%) was greater than that of combination (55,92±16,35%). The effect of combination of C.xanthorrhiza extract and A.paniculata extract on the GB contraction was much less than the effect of each extract administered separately. This study shows that the combination of C.xanthorrhiza extract and A.paniculata extract did not increase the gallbladder contraction (much less than the effect of each extract administered separately).

Keyword: Cholekinetic, Curcuma xanthorrhiza, Andrographis paniculata, extract Gallbladder Contraction (GBC)

INTRODUCTION
Temulawak (C.xanthorrhiza) and Sambiloto (A. paniculata) is traditionally consumed by Indonesian people and believed to have a beneficial effect on health. Sambiloto (A. paniculata) and Curcumin an active compound found C.xanthorrhiza have the cholekinetic effect on healthy human gallbladder (Rangkuti, 2006; Rasyid et al., 1999).

These finding shows that these two medicinal plants may be useful in preventing gallbladder stone formation. It is well known the lack motility of gallbladder is a factor causes stone formation (Ooi et al., 2004). By enhancing the contraction of gallbladder biliary flow will be increased or the biliary sludge will push out from the gallbladder.

Nowadays there are some products known as jamu combine these two medicinal plants. However, there is no evidence yet whether this combination will increase the cholekinetic effect compare to administering one of them. The aim of the present study is to compare the cholekinetic effect produced by single dose of C.xanthorrhiza extract and A.paniculata extract administered separately or in combine on healthy adult volunteers.

MATERIALS AND METHODS
The present study was conducted using the method of Rasyid and Lelo (2002). A randomized, double blind, and crossover design with a wash-out period of one week was carried out in 6 healthy volunteers (4 males; 2 females), aged: 21-26 years (22.17±2.40 years) with body weight 48.5-63 kg (54.75±4.83 kg) and heights ranging from 154 to 170 cm (mean ± SD 163 ±0.05 cm). All subjects received their informed written consent to participate in the study.

The study protocol was approved by the Dean of the School of Medicine and The University Research Committee of University of Sumatera (Institutional Ethics Committee), Medan, Indonesia. All subjects were evaluated for general good health on the basis of medical history, physical examination, laboratory tests and ultrasonography of the upper abdomen.

None of subjects had a history or clinical evidence of hepatobiliary or gastrointestinal disease or operations. None of them took any regular medication (including 'jamu' and oral contraceptive pills) for at least 7 days prior of the study. nor were they permitted to have fatty meals before the study. The subjects were all in good health with no jaundice and unpalpable liver and spleen. Bilirubin, Serum Glutamic Oxaloacetic
Transaminose (SGOT), Serum Glutamic Pyruvic Transaminose (SGPT), alkaline phosphates, cholesterol, albumin and globulin levels were normal. Ultrasonography of the upper abdomen showed normal liver, gallbladder and biliary tract. The subject who had the ellipsoid form of gall bladder was able to participate in this study (Rasyid A, et al. 2002).

The present study consist of three treatment, they are 40 mg of Curcuma xanthorrhiza extract, 20 of Andrographis paniculata extract and combination of 40 mg of Curcuma xanthorrhiza extract and 20 mg of Andrographis paniculata. Extract formulated in the same capsule was swallowed with 100 ml water. The Curcuma xanthorrhiza extract and Andrographis paniculata extract used in this study was purchased from C.V. Herba Medica Centre (Perusahaan Jamu Siti Ara), Batu, East Java, Indonesia.


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GV = 0.52 \times \text{length} \times \text{width} \times \text{depth}
\]

Three diameters (length, width and depth) of the gallbladder were measured by using an ultrasound machine with a real-time system model SSHI 140 A (Toshiba, Shimoishigami Ottawara, Japan) which have a 3.75 MHz convex sector transducer similar to the one used in other studies (Sharma, et al. 1995, Schedermairer, et al, 1997). The gallbladder contraction was calculated based on GBV changes, it was recorded as the percentage reduction in gallbladder volume (% GBV) compared to the fasting gall bladder volume (GBV0).

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\%GBV = \left( \frac{GBV_{0}-GBVi}{GBV_{0}} \right) \times 100\%
\]

Where GBV0 = fasting gall bladder volume and GBVi = gall bladder volume at the time measured. If gall bladder reduction was observed it was noted as positive contraction.

After fasting for a period of ± 10 hours, on the day of examination, before taking the medicine the Gallbladder Volume (GBV) was ultrasonographycally measured, then the GBV was serially measured at 0.5, 1.0, 1.5 and 2 hours after administration of 40 mg Curcuma xanthorrhiza extract, 20 mg of Andrographis paniculata extract and combination of 40 mg of Curcuma xanthorrhiza extract and 20 mg of Andrographis paniculata extract.

The transducer was placed in a sagittal plane in the right upper quadrant of the supine subject with the left lateral decubitus 45-degree position. Each subject was required to hold a maximum deep thoracic inhalation for maximal visualization of the gallbladder, and for standardization of gallbladder measurements (Rasyid and Lelo, 1998). Data obtained were expressed as mean ± standard deviation and analyzed using one way ANOVA, P value < 0.05 regarded as statistically significant.

RESULTS AND DISCUSSION

The fasting GBV before taking 40 mg Curcuma xanthorrhiza extract (10.80 ± 3.45 mL), 20 of Andrographis paniculata Extract (10.41 ± 2.34 mL) and combination of 40 mg of Curcuma xanthorrhiza Extract and 20 mg of Andrographis paniculata Extract (10.48 ± 3.86 mL), GBV was reduced over the 2 h observation time after each treatment, and significantly different (p<0.01) for time based comparison, but there was no statistically different (P>0.05) for treatment comparison (Table 1).

On the other hand the gallbladder contraction (GBC) were increase with the time and significantly different either based on time or treatment. For treatment based comparison the GBC was significantly different at 1 and 1.5 h of observation time. The percentage of GB contraction at 2 h after administration of 20 mg A. paniculata (74.58± 8.27%) or 40 mg C. xanthorrhiza extract (71.93±13.43%) was greater than that of combination (55.92±16.35%) (Table 2).
Table 1. Gall bladder volume after administration of 40 mg C. xanthorrhiza, 20 mg A. paniculata and combination of 40 mg C. xanthorrhiza and 20 mg A. paniculata

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Time (h)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.0</td>
<td>0.5</td>
</tr>
<tr>
<td>40 mg C. xanthorrhiza</td>
<td>10.80±3.45</td>
<td>6.65±3.79</td>
</tr>
<tr>
<td>20 mg A. paniculata</td>
<td>10.41±2.34</td>
<td>5.84±1.28</td>
</tr>
<tr>
<td>40 mg C. xanthorrhiza + 20 mg A. paniculata</td>
<td>10.48±3.86</td>
<td>7.36±2.54</td>
</tr>
<tr>
<td>P-value</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Table 2. Percentage of gall bladder contraction after administration of 40 mg C. xanthorrhiza, 20 mg A. paniculata and combination of 40 mg C. xanthorrhiza and 20 mg A. paniculata

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Time (h)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.5</td>
<td>1.0</td>
</tr>
<tr>
<td>40 mg C. xanthorrhiza</td>
<td>40.92±16.95</td>
<td>51.63±16.64</td>
</tr>
<tr>
<td>20 mg A. paniculata</td>
<td>41.87±15.82</td>
<td>61.50±8.86</td>
</tr>
<tr>
<td>40 mg C. xanthorrhiza + 20 mg A. paniculata</td>
<td>28.68±8.28</td>
<td>42.74±7.19</td>
</tr>
<tr>
<td>P-value</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
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Figure 1. Percentage of gall bladder contraction after administration of 40 mg C. xanthorrhiza, 20 mg A. paniculata and combination of 40 mg C. xanthorrhiza and 20 mg A. paniculata

This study showed that administration of 40 mg Curcuma xanthorrhiza extract combining with 20 mg of Andrographis paniculata extract did not produce greater contraction compared to 40 mg Curcuma xanthorrhiza extract or 20 mg of Andrographis paniculata administered separately (fig.1).

This phenomenon may be caused by each extract not working at the same time, when the gallbladder contraction occurred as a cholekinetic effect of Andrographis paniculata extract another one (Curcuma
xanthorrhiza extract) cannot give its maximum cholekinetic effect because the gallbladder muscle is already in spasm state.

CONCLUSIONS
Combination of 40 mg Curcuma xanthorrhiza extract and 20 mg of Andrographis paniculata extract did not increase gallbladder contraction compare to each extract administered separately.

REFERENCES