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Pharmacokinetic interaction between irbesartan and *Orthosiphon stamineus* extract in rat plasma

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Orthosiphonstamineus commonly known as kumis kucing has been used traditionally for rheumatoid, gout, renal calculus, hypertension, diabetes, etc. [1]. It is often used in combination with synthetic hypertensive drugs like irbesartan. However, both effectiveness combination herbal medicine with modern pharmaceuticals, and the possible adverse effects from herb–drug interactions remain to be verified.

This study investigated effect of *O. stamineus* extract to pharmacokinetics of irbesartan co-administration in *Sprague Dawley* rats. After *O. stamineus* extract pretreatment (500 mg/kg BW) for 6 days orally, on the seventh day rats were administered irbesartan (40 mg/kg BW) orally, then the blood sample were collected into heparinized tube via sinus orbitalis at 0, 0.5, 1, 1.5, 2, 2.5, 3, 4, 8, 12, 24 and 36 hours after drug administration, then centrifuged at 10,000 rpm for 10 minutes to separate out plasma. The rat plasma was extracted by protein precipitation with acetonitril and analyzed by liquid chromatography tandem mass spectrometry, with an electrospray ionization (ESI) source at positive ion mode in the multiple reaction monitoring (MRM), was detected at m/z 429.1 > 205.9 (for irbesartan), m/z 373 > 342.9 (for sinensetin) and m/z 423.05 > 404.9 (for losartan as internal standard). The plasma concentration irbesartan in the group combination of irbesartan and extract of *O. stamineus* was 4843.25 ng/mL and half time was 32.07 hours, higher and prolonged than the group irbesartan alone (2426.20 ng/mL and 23.82 hours). The pharmacokinetic profiles are in Fig. 1. According to the *in vitro* study it was shown that the extract of *O. stamineus* has potent inhibitory activity against CYP2C9 [2], so the herb–drug interaction mechanism may be due to the inhibitor of CYP2C9, because irbesartan is also metabolized by CYP2C9. The results showed that concomitant use of irbesartan and extract of *Orthosiphon stamineus* increased the plasma level (*Cmax*) and prolonged the half life (t1/2) of irbesartan.

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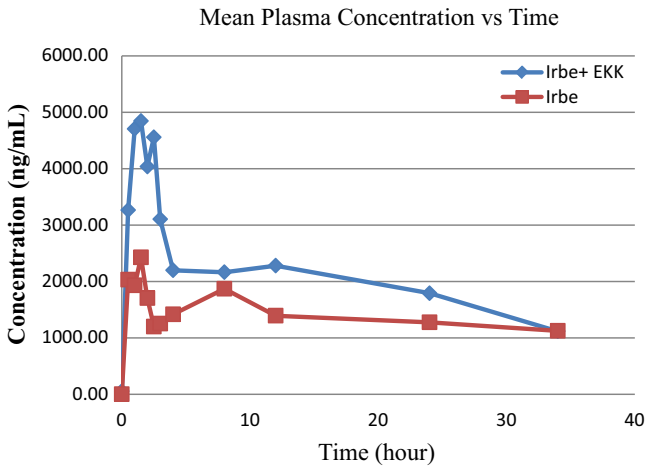

Fig. 1 – The pharmacokinetic profile of irbesartan alone (*n* = 5) and irbesartan + extract of *O. stamineus* (*n* = 5).

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