Author’s response to reviews

Title: Fructus Ligustri Lucidi Modulates Estrogen Receptor Expression With No Uterotrophic Effect in Ovariectomized Rats

Authors:
Yuqing Tang (tangyuqing@live.com)
Cheng Li (celialee_cheng@163.com)
Xuejiao Sun (1099648128@qq.com)
Yi Liu (18674852163@163.com)
Xiting Wang (wxtlofe@163.com)
Yubo Guo (1264115049@qq.com)
Lili Wang (wangxiaoxing0108@163.com)
Rufeng Ma (marufeng5188@126.com)
Jianzhao Niu (niujianzhao@126.com)
Min Fu (fumin1025@gmail.com)
Dongwei Zhang (zhdw1006@163.com)
Yu Li (liyubeijing1973@163.com)

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Fructus Ligustri Lucidi Modulates Estrogen Receptor Expression with No Uterotropic Effects in Ovariectomized Rats

Yuqing Tang; Cheng Li; Xuejiao Sun; Yi Liu; Xiting Wang; Yubo Guo; Lili Wang; Rufeng Ma; Jianzhao Niu; Min Fu; Dongwei Zhang, Ph.D.; Yu Li, Ph.D.
Response: Thanks for your comments. The water extract of FLL is demonstrated to improve bone microstructures and bone metabolism in OVX rats. The results have been published in the journal of Chinese traditional and herbal Drugs (GUO Yu-bo, WANG Li-li, MA Ru-feng, WANG Liang, YANG Mei-juan, TANG Yu-qing, LIU Chen-yue, ZHU Ru-yuan, LIU Hai-xia, ZHAO Dan-dan, MO Fang-fang, NIU Jian-zhao, GAO Si-hua, LI Yu, ZHANG Dong-wei. Effects of water extract from Ligustri Lucidi Fructus on bone structure and metabolism in ovariectomized rats. Chinese Traditional and Herbal Drugs. 2016,7(47) :1155-1162). In addition, the ancient Chinese medicinal literature indicates that decoction was often used to process Chinese herbs in the clinical treatment. The oral administration used in the current study is most accepted in traditional Chinese medicine and may truly reflect the effect of Chinese herbs.

In the previous studies, we demonstrated that FLL water extracts mainly contain salidroside, ligustroflavon, acteoside, specnuezhenide, and oleuropein acid. water-soluble protein, triterpenoid saponins, flavonoids and their glycosides, dihydro-anthaquinones, volatile oils, polysaccharides, and polyphenols, which is determined by HPLC-DAD–ESI-MS.

Question 2. Why did you use only one concentration? Why did you choose that concentration?

Response: Thanks for your valuable question. The concentration used in the current study has been demonstrated to be effective in preventing the development of osteoporosis in rats (Chinese Traditional and Herbal Drugs. 2016,7(47) :1155-1162). In addition, the concentration of FLL in the current experiment is equivalent to the clinical doses of adults used in the treatment of osteoporosis.

Reviewer reports:

Osteoporosis is one kind of the most common bone remodeling diseases characterized by reduction of bone mass and microstructural deterioration of bone tissue. Fructus Ligustri Lucidi (FLL) documented to be used to strengthen bone and treat osteoporosis for a long time in China. The present study aimed to investigate the effect of FLL on ERα and ERβ expressions in bone and uterus of OVX rats. The experimental design is straightforward, and data are clearly presented. The result could provide scientific data for modern utilization of FLL. However, to my knowledge, salidroside, hydroxytyrosol, and specnuezhenide are the major active components of FLL. Especially, salidroside has been proven to be very effective in treatment of osteoporosis. So, I suggested that authors should improve the discussion with the published phytochemical researches.

Response: Thanks for your comments. We have improved the discussion in the revised version. (Discussion section, Paragraph 6, page 11).
Furthermore, the major active components of FLL include salidroside, nuzhenide, specnuezhenide, hydroxytyrosol, oleanolic acid, ursolic acid, acetyl oleanic acid, and quercetin. Salidroside is able to increase BMD, alkaline phosphatase (ALP) activity, and reduced glutathione (GSH) concentration, and decrease osteoclast differentiation inducing factors and the production of intracellular reactive oxygen species (ROS) [39] in OVX mice and rats [40]. Oleanolic acid is demonstrated to reverse bone loss by increasing osteoblastogenesis [41] and inhibiting osteoclastogenesis [42, 43]. Ursolic acid can promote osteoblastic differentiation and mineralization [44]. Hydroxytyrosol is also demonstrated to inhibit osteoclast activation and reverse bone loss in OVX mice [45]. The above-mentioned ingredients may account for the anti-osteoporotic effect of FLL in OVX rats. However, further studies are still needed to identify active components in the FLL water extract.