Does horny goat weed have any clinically significant interactions?

Prepared by UK Medicines Information (UKMi) pharmacists (or other as appropriate) for NHS healthcare professionals
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Background

Horny goat weed (Epimedium.) is a herbaceous flowering plant (1). In the past horny goat weed has been used as an anti-rheumatic, a general tonic, and to improve bone health and treat osteoporosis. Currently it is more commonly used to treat sexual dysfunction such as impotence and involuntary ejaculation (2, 3).

Horny goat weed is known by several names including Yin Yang Huo, Inyokaku and Herba Epimedii. It is associated with several species including Epimedium sagittatum, Epimedium grandiflorum and Epimedium brevicornum. Usually, a mixture of species is present in traditional Chinese herbal medicines (3).

In common with most herbal medicines, many of the active constituents remain largely unknown, along with their pharmaceutical relevance. It is thought that the major constituents are prenylated flavonoids and isoflavones. Of these, the most relevant are quercetin, icriin, epimedin A, B and C and 6 prenylchrysin, which are thought to produce the pharmacological activity of horny goat weed (3). Icariin is known to have phosphodiesterase activity (4).

Answer

There is often a paucity of information available about herbal medicines. The lack of a documented interaction does not necessarily mean no interaction exists; it may just mean that this combination of herb and conventional pharmaceutical have not been used together before (5).

There are no published interaction studies in humans. *In vitro* data suggest that interactions could occur. Interactions due to additive pharmacological effects may also be possible. A summary of potential interactions with horny goat weed is presented in Table 1.

N.B. This is not an exhaustive list, and many interactions included in the list have been extrapolated from in vitro studies and theoretical information. Not all medicines metabolised by hepatic enzymes inhibited by horny goat weed are included. Readers are advised to check individual medicines summary of product characteristics for biotransformation information.

Table 1. Potential interactions of horny goat weed (4, 6, 7, 8, 9, 10, 11, 12, and 13)

Interaction	Severity	Possible mechanism	Notes
Warfarin	Unknown	Inhibition of CYP1A2 and CYP2C9 Quercetin shares a binding site on human serum albumin	May increase levels and lead to an increased risk of bleeding
Clopidogrel	Unknown	p-glycoprotein inhibition	Animal studies suggest a potential interaction in rats
Amitriptyline	Unknown	Inhibition of CYP1A2, CYP2C19 and CYP2D6,	May increase levels and increase the risk of adverse drug reactions i.e. QT

		CYP2C9 & CYP3A4	prolongation as an additive effect.
Drugs that prolong the QT interval	Unknown	Additive effect	QT prolongation reported
Ciclosporin and tacrolimus	Unknown	Inhibition of CYP3A4	May increase levels and increase risk and adverse reactions. Ciclosporin and tacrolimus are CYP3A4 inhibitors. Ciclosporin also acts as p-glycoprotein inhibitor.
Phenytoin	Unknown	Inhibition of CYP2C19	May increase levels and increase risk of adverse effects and toxicity due to narrow therapeutic index
Clarithromycin and erythromycin	Unknown	Inhibition of CYP3A4	May increase levels and increase risk of adverse drug reactions
Phosphodiesterase type-5 (PDE-5) inhibitors (sildenafil. tadalafil, vardenafil)	Unknown	Additive effect	Icariin component inhibits PDE-5 *in vitro.* Risk of additive and prolonged and/or enhanced effects.
Glyceryl trinitrate and other nitrates	Unknown	Hypotension	Icariin component is a phosphodiesterase-5 inhibitor. Co-administration of phosphodiesterase-5 inhibitor and nitrate is considered a contraindication due to the risk of severe hypotension.
Drugs causing hypotension	Unknown	Hypotension	Risk of additive hypotension
Oestrogen	Unknown	Additive effect	Horny goat weed may have oestrogenic activity and increase oestrogen levels in some women
Adriamycin, vincristine, cisplatin, 5-fluorouracil	Unknown	p-glycoprotein inhibition	Significantly increases the cytotoxicity in MDR HepG2/ADR (liver cancer cell line). Icaritin down-regulates expression of P-glycoprotein via decreasing the expression of MDR1 gene.

Adverse reactions

A case report of a 66-year-old man, presenting with tachyarrhythmia and hypomania required hospital treatment after taking a horny goat weed extract tablet product for two weeks to enhance sexual function (12). Other adverse reactions reported include dizziness, vomiting, dry mouth, thirst and nose bleeds. Patients taking high doses of horny goat weed have reported more serious adverse reactions, including respiratory arrest and increased tendon reflexes causing spasm (2). In one case, QT prolongation, which can pose an increased risk of sudden death, has been reported, It is,

however, not clear in this case report whether horny goat weed was responsible as the product taken was a combination product containing a wide range of other herbs (7).

Summary

Horny goat weed (Epimedium) is a herbal medicine that may comprise of mixtures of different related *Epimedium* species, which contain numerous and varied active constituents. As herbal products are subject to variations in quality, safety and efficacy, their use should not be recommended routinely.

There is no published human information on drug interactions with horny goat weed. There is, however, the potential for significant drug interactions due to its inhibitory action on certain subgroups of the cytochrome P450 enzyme system, although the degree to which it does so is currently unknown. Drugs with which horny goat weed may interact via this mechanism include warfarin, amitriptyline, clarithromycin and erythromycin, ciclosporin and tacrolimus, and phenytoin. Furthermore, horny goat weed may enhance or prolong the effects of drugs that prolong the QT interval, and there is a potential for an additive interaction with phosphodiesterase-5 inhibitors for erectile dysfunction.

Due to the lack of information of the nature and extent of interactions of horny goat weed in humans, it would be prudent to advise patients to avoid use of the product concurrently with medication until it is more widely studied.

Limitations

This Q&A considers only drug interactions with horny goat weed. It does not take into account efficacy data, which would need to be considered when treatment decisions are being undertaken. The amount of good quality information available about herbal medicines is often limited due to the lack of regulation of these products. Many of the safety concerns are theoretical or are based on case reports only.

Some interactions are based on the extrapolation of findings from in vitro studies on isolated enzymes.

References

1. The Royal Horticultural Society. April's Plant of the Month [Internet] 2015. [Date accessed: 14th May 2020]. URL: https://www.rhs.org.uk/gardens/hyde-hall/hyde-hall-blogs/hyde-hall/april-2015/april-plant-of-the-month
2. The Natural Medicines Comprehensive Database. Horny Goat Weed Monograph [Internet] [Date accessed: 30th August 2019]. URL: https://naturalmedicines.therapeuticresearch.com
3. Williamson E, Driver S, Baxter K (eds). Epimedium Monograph. In: Stockley's Herbal Medicines Interactions. [online] London: Pharmaceutical Press. [Date accessed: 14th May 2020]. URL: http://www.medicinescomplete.com/
4. Ning H, Xin ZC, Lin G et al Effects of icariin on phosphodiesterase – 5– activity in vitro and cyclic guanosine monophosphate level in cavernous smooth muscle cells. Urology 2006; 68: 1350-1354
5. NHS Health A – Z. Herbal medicines. {Internet] 2018. [Date accessed 14th May 2020]. URL: https://www.nhs.uk/conditions/herbal-medicines/
6. Liu KH, Kim MJ, Jeon BH Et Al Inhibition of human cytochrome P450 isoforms and NADPH-CYP reductase in vitro by 15 herbal medicines including Epimedii Herba. Journal of Clinical Pharmacy and Therapeutics. 2006; 31, 83-91
7. Phillips M, Sullivan B, Snyder B et al The effect of Enzyte ® on QT and QTc intervals. Archives of Internal Medicine. 2010; 170(15): 1402-1405
8. Electronic Medicines Compendium. Summary of Product Characteristics Viagra 25mg film-coated tablets [Internet] 2020. [Date accessed 14 May 2020]. URL: https://www.medicines.org.uk/emc/product/1072/smpc
9. Cirigliano MD, Szapary PO. Horny goat weed for erectile dysfunction. Alt Med Alert 2001;4:19-22

10. Agli MD, Galli GV , Cero ED et al potent inhibition of human phosphodiesterase-5 by icariin derivatives. Journal of Natural Products. 2008; 71: 1513-1517
11. Lee J, Shin Y,et al. Pharmacokinetic interactions of clopidogrel with quercetin, telmisartan, and cyclosporine A in rats and dogs. Archives of Pharmacal Research 2012; 35(10): 1831-1837
12. Partin JF, Pushkin YR Tachyarrhythmia and hypomania with horny goat weed. Psychosomatics 2004; 45(6): 536.
13. Dewanjee S, Dua TK , Bhattacharjee N et al., (2017) 'Natural Products as Alternative Choices for P-Glycoprotein (P-gp) Inhibition', Molecules, 22(871), pp. doi:10.3390/molecules22060871.

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