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Weige

Treatment of Erectile Dysfunction

Chinese herbal medicine whose main bioactive constituent is dehydrocorydaline

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Introduction

Penile erection is initiated when, under parasympathetic influence, the sinusoids and cavernosal and helicinal arteries dilate with a subsequent increase in blood flow to the lacunar spaces of the corpus cavernosum. Relaxation of the trabecular smooth muscle then follows, expanding and compressing the plexus of subtunical venules against the tunica albuginea, thus reducing venous outflow and increasing intracavernous pressure, leading to penis engorgement and erection (1). Sildenafil, a drug approved by the U.S. Food and Drug Administration in 1998 for the treatment of male erectile dysfunction, increased intracavernosal pressure in experimental animals via relaxation of trabecular smooth muscle and improved erections in patients with erectile dysfunction (2, 3). Although sildenafil has been associated with postmarketing cardiovascular adverse events, it is still considered safe and effective if used according to new warnings and information in the product labeling (4, 5). Nevertheless, there is still a need for novel male potency drugs with high efficacy and low toxicity. Weige, a Chinese herbal medicine, was recently found in a series of animal experiments and preliminary clinical trials to be effective in erectile improvement (6) and has the potential to be developed as a new compound for the treatment of male erectile dysfunction.

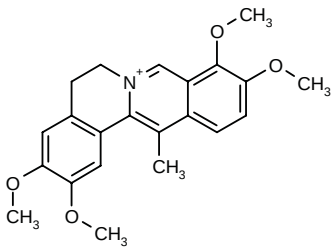
Physiochemical Properties

Weige is composed of several Chinese herbal medicines. Dehydrocorydaline [I] is its main bioactive constituent. Dehydrocorydaline can be isolated from several plants, including *Corydalis yanhusuo* W.T. Wang, *Corydalis ambigua* Cham. et Schlecht. var. amurensis Marxim., *Corydalis ambigua* Cham. et Schlecht. and *Corydalis pallida* Pers var. tenuis Yatabe. Its chemical structure is very similar to sildenafil (7).

Pharmacological Actions

In male mice, weige increased intimate action more markedly than sildenafil (Table I). Bioactive comparison between weige and sildenafil in male rats also indicated that weige was more effective than sildenafil in shortening the latent period of climbing and striding, the starting time of sexual excitement and latent period of ejaculation. The frequency and number of penetrations were also significantly increased in weige-treated animals as compared to the sildenafil-treated group (8) (Table II).

In mice, the acute lethal doses of dehydrocorydaline were 277 (p.o.), 21 (i.p.) and 8.8 (i.v.) mg/kg, respectively. When rats were administered dehydrocorydaline at doses of 15 mg/kg i.p. for 20 days or at 50 mg/kg p.o. for 30 days, there were no significant changes in hematol-



[I]

Table I: Effect of weige on sexual activity of male mice.

Group	Intimate action	% Enhancement
Vehicle	20	–
Weige	52	160
Sildenafil	40	100

Table II: Effect of weige on erectile function of male rats.

Group	LPCS	STSE	LPE	FP	NP
Weige	↓↓↓	↓↓↓	↓↓↓	↑↑↑	↑↑↑
Sildenafil	↓↓	↓↓	↓	↑↑	↑↑

LPCS: latent period of climbing and striding. STSE: starting time of sexual excitement. LPE: latent period of ejaculation. FP: frequency of penetration. NP: number of penetrations. ↓: decrease. ↑: increase.

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ogy, serum chemistry or urinalysis tests and no changes in the morphology of vital organs, indicating that weige may be relatively safe in clinical practice. Preliminary pharmacokinetic studies indicated that the onset of action of weige was very rapid, similar to that of sildenafil, although its duration of action was much longer than sildenafil (8).

The mechanism of action of weige is not yet clear. It is known that the peripheral nervous control of relaxation of trabecular smooth muscle is dependent on the interaction between adrenergic, cholinergic and nonadrenergic noncholinergic (NANC) mechanisms (9, 10). Recently, nitric oxide was identified as an important neurotransmitter involved in NANC neutrally mediated cavernosum relaxation (11). Nitric oxide causes relaxation by activating soluble guanylate cyclase, resulting in accumulation of intracellular guanosine 3':5'-cyclic monophosphate (cGMP) (12). Cyclic GMP appears to elicit relaxation of smooth muscle by lowering the intracellular Ca^{2+} concentration through stimulation of sarcoplasmic Ca^{2+}-ATPase activity or through the opening of K^+ channels leading to hyperpolarization (13). Thus, it is clear that cGMP is an important intracellular messenger in trabecular smooth muscle cells and is involved in NANC relaxation of erectile tissues of the penis. Recent studies demonstrated that cultured human corpus cavernosum smooth muscle cells expressed phosphodiesterase type V activity which was inhibited by nanomolar concentrations of sildenafil (14). It was suggested that sildenafil could cause the accumulation of intracellular cGMP via inhibition of phosphodiesterase activity and result in further relaxation of erectile tissues. Dehydrocorydaline, a main constituent of weige, was shown to relax smooth muscle by increasing cGMP levels in smooth muscle cells (15). Therefore, weige-mediated relaxation of erectile tissues may also be associated with increases in cGMP levels (8). The similarity in the structures of dehydrocorydaline and sildenafil may contribute to their similar mechanisms of action.

Clinical Studies

In a double-blind study in China in 308 male patients with erectile dysfunction due to organic, psychogenic or mixed causes such as traumatic spinal cord injury, weige administered orally before sexual activity was shown to improve the ability to achieve and maintain an erection. Mean scores for frequency of penetration, frequency of maintained erections and sexual satisfaction were consistently higher in patients treated with weige compared with the placebo-treated group. The overall intercourse satisfaction rate for weige was 92%, which was superior to that of sildenafil (70%) (15, 16).

Conclusions

Results from a series of experimental studies evaluating the effects of weige on erectile function indicate that the agent could enhance sexuality. A preliminary clinical trial also revealed that treatment with weige results in an improvement in sexual satisfaction. Moreover, weige appears to be more effective than sildenafil. Since weige is a complex prescription consisting of Chinese herbal medicines, in contrast to sildenafil which is a pure compound, it may be better tolerated by patients. Thus, weige may prove to be more versatile than sildenafil. However, more extensive clinical trials are needed to further determine the efficacy and safety of weige in the treatment of male erectile dysfunction.

Manufacturer

Shenyang Feilong Health Products Co. Ltd. (CN).

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