

# Yohimbine: Old Drug with New Interactions

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Yohimbine is an alkaloid derived from the bark of a tree from West Africa and has been used to treat various types of sexual dysfunction. It has also been used to treat tricyclic antidepressant-induced hypotension, and when combined with the norepinephrine uptake inhibitor atomoxetine (Strattera), yohimbine has recently been found to be helpful in treating hypotension in patients with peripheral autonomic failure.<sup>1</sup> Yohimbine is available as a prescription, but it is much more commonly found in a variety of herbal products that are advertised for erectile dysfunction and for sexual dysfunction caused by selective serotonin reuptake inhibitors.

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## How Does Yohimbine Interact?

Alpha<sub>2</sub>-adrenergic (A2A) receptors are involved in regulation of synaptic norepinephrine concentrations in the peripheral sympathetic system. Yohimbine inhibits A2A receptors, which increases sympathetic outflow leading to increased synaptic norepinephrine. Yohimbine, therefore, may

have additive or antagonistic effects with other drugs that stimulate or inhibit A2A receptors, or otherwise affect synaptic norepinephrine concentrations.

## Anti-Clonidine Effects

Clonidine (eg, Catapres) stimulates A2A receptors and thereby reduces sympathetic outflow and reduces synaptic norepinephrine. Yohimbine does the opposite; it is an A2A receptor antagonist, and would be expected to inhibit clonidine effects. This interaction is based largely on theoretical considerations, but it seems likely that yohimbine would inhibit the antihypertensive effects of clonidine. Yohimbine probably also inhibits the antihypertensive effects of drugs related to clonidine, such as guanabenz and guanfacine.

## Effects with Norepinephrine Reuptake Inhibitors

Given the ability of yohimbine to inhibit A2A receptors and increase synaptic norepinephrine, it would be expected to have additive effects with drugs that inhibit norepinephrine reuptake. As mentioned above, yohimbine enhances the hypertensive effect of atomoxetine in patients with inadequate synaptic norepinephrine.

Yohimbine may also interact with other norepinephrine reuptake inhibitors, such as tricyclic antidepressants, and serotonin-norepinephrine reuptake inhibitors, including clomipramine (Anafranil), desvenlafaxine (Pristiq), duloxetine (Cymbalta), imipramine (Tofranil), milnacipran (Savella), and venlafaxine (Effexor).

This may have a positive effect in some patients, as shown by a study in which yohimbine improved blood pressure in patients with clomipramine-induced orthostatic hypotension.<sup>2</sup> But it is also possible that some patients given yohimbine and

norepinephrine reuptake inhibitors may manifest excessive increases in blood pressure, especially when they are supine.

## Interactions with MAOIs

Nonselective monoamine oxidase inhibitors (MAOIs), such as phenelzine (Nardil) and tranylcypromine (Parnate), increase norepinephrine stores in peripheral adrenergic neurons, and theoretically would have additive effects with yohimbine, which increases sympathetic outflow to these neurons. A hypertensive crisis is possible. This potential interaction is based primarily on theoretical considerations, but it appears likely that it would occur. Yohimbine may also interact in patients receiving other MAOIs, such as furazolidone or methylene blue.

## Summary

Yohimbine is likely to inhibit the antihypertensive effects of clonidine, guanabenz, and guanfacine. It would be prudent to advise patients taking these antihypertensives to avoid yohimbine products. If yohimbine is used with these drugs, the blood pressure should be carefully monitored.

Yohimbine may interact with drugs that inhibit synaptic norepinephrine uptake to produce an excessive increase in blood pressure. (This interaction may be favorable in patients with tricyclic antidepressant-induced orthostatic hypotension, but the blood pressure should be monitored closely if yohimbine is used for this purpose.)

Patients with antidepressant-induced sexual dysfunction should be advised to consult with their physician before taking yohimbine products to treat it. Patients taking MAOIs should be advised to completely avoid yohimbine-containing products. ■

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