hormone and promote sleep that tends to be deeper and less fragmented. I tend not to prescribe quick-release melatonin preparations, since they rapidly increase blood levels but do not promote a more restful and longer sleep. On occasion, I will combine a small dose (1 mg) of quick-release melatonin with a controlled- or prolonged-release preparation (3–6 mg), to facilitate quick sleep onset with sustained hormone levels to offset a broad array of sleep issues (e.g., racing mind, restlessness, and waking too early) that patients tend to experience during the tapering process.

Niacinamide (nicotinamide) can also be given to reduce withdrawal symptoms from all psychotropic drugs, since it generally "calms" the nervous system and does not possess any concerning drug interactions. It is sometimes very useful among patients withdrawing from benzodiazepines, since it possesses benzodiazepine-like effects.[14] One case report demonstrated its clinical effectiveness in allowing a patient to remain clinically stable while tapering off clonazepam.[14] The patient weaned himself off clonazepam in 2 weeks while increasing his daily amounts of niacinamide until he was taking 2500 mg each day. When this report was published, the patient had been free of clonazepam for 6 months and had remained stable on only the niacinamide. A written correspondence from the late Dr. William Kaufman (January 10, 1998) noted the following about the vitamin's mechanism of action:

> Niacinamide has ungated access to the brain. When it enters the brain, it has a strong affinity for the benzodiazepine receptors and causes a desirable calmative effect which you have observed. But it also improves other functions of the central nervous system.

Effective daily doses of niacinamide range from 1500 to 2500 mg. It is rarely necessary to go beyond 2500 mg, since higher doses can be associated with nausea and potentially vomiting. The mean elimination half-life in human subjects given 3000 mg of the vitamin was 5.9 ± 0.6 hours.[15] Since it has such a short elimination half-life, niacinamide must be administered several times throughout the day; otherwise, its therapeutic effects will be lessened.

To stabilize mood resulting from withdrawal and to ease mood swings during tapering, I use a product called Neurapas Balance. Its therapeutic effects limit anxiety, depression, muscle tension, stress reactions, and other withdrawal reactions resulting from the tapering process. Each film-coated tablet contains 60 mg of the dry extract of *Hypericum perforatum*, 28 mg of the dry extract of *Valerian officinalis*, and 32 mg of *Passiflora incarnata*. There have been approximately 10 company-sponsored clinical studies (i.e., 2 controlled and 8 observational cohort studies) and 2 experience reports, which have shown this herbal combination to be safe and effective for both depression and anxiety.[16] Each individual herbal extract possesses well-known postulated mechanisms of action.[17] The extract of *Hypericum perforatum* exhibits monoamine oxidase inhibition, gamma-aminobutyric acid (GABA) activity, monoamine reuptake, upregulation of 5-hydroxytryptamine 1A (5-HT1A) and 5-HT2A receptors, and modulation of cytokine production. Valerian is known to have GABAergic effects. *Passiflora* is a partial agonist to benzodiazepine receptors. Generally, my patients start with 1 pill twice daily, and over the course of many weeks, the dose is increased to 3 pills twice daily. Even though the elimination half-life is not known for this preparation, multiple daily dosing appears to yield more optimal therapeutic outcomes.

Clinicians should not be overly concerned about adverse drug interactions, since this specific preparation contains a very low daily dose of *Hypericum* (i.e., 360 mg from 6 tablets) with a correspondingly low hyperforin content.[18] Studies demonstrating significant pharmacokinetic drug interactions with *Hypericum* extracts typically involve daily dosages of 900 mg or more. At the recommended daily dose of 6 tablets, the mean amounts of hypericin and hyperforin delivered are 0.72 mg and 1.35 mg respectively. This small amount of hyperforin does not induce the major liver drug-metabolizing enzyme cytochrome P(CYP)450 3A4. *Hypericum* preparations containing much higher amounts of hyperforin do induce this enzyme, and those are believed to be the reason for numerous potential drug interactions. Unfortunately, the low-dose preparation is not available in the US.

Rhodiola rosea extract can also stabilize patients during psychotropic tapering. Clinical trials have shown it to attenuate mild and moderate depression, generalized anxiety, and burnout/fatigue – common withdrawal symptoms that many patients experience during tapering.[19–21] It specifically works by inhibiting enzymes involved in the degradation of monoamine neurotransmitters (i.e., serotonin, dopamine, and norepinephrine), and this prevents the depletion of adrenal catecholamines following acute stress.[22] The therapeutic dose range is somewhere between 500 and 680 mg of a standardized extract containing 3% percent total rosavins and 1% salidrosides. I normally recommend that *Rhodiola rosea* extract to be taken with breakfast, as it can cause considerable nausea and possibly vomiting on an empty stomach. I usually prescribe 500 mg at breakfast to stabilize mood and lessen anxiety, and will increase the daily dose to 650 to 680 mg if the patient's response is not marked enough. Although a rat study determined the elimination half-life of salidroside in *Rhodiola rosea* extract to be 39.69 ± 21.02 minutes, I have not found multiple dosing throughout the day necessary.[23] I doubt that the elimination half-life from the rat study correlates to the elimination half-life in humans.

There is one published report of an interaction between *Rhodiola rosea* extract and escitalopram.[24] The case involved a 26-year-old Chinese female who presented to the emergency department with a 1-hour history of heart palpitations and light-headedness. The patient was diagnosed with supraventricular tachycardia (SVT) as per electrocardiogram findings. Her pulse rate was 150 beats per minute, and her troponin I was significantly elevated (0.39 mg/L; normal < 0.06). All other investigations were normal. She was treated with 6 mg of intravenous adenosine, which normalized her sinus rhythm. No more SVTs happened at follow-up, and her troponin I normalized in 2 days. While this case points to possible interactions between *Rhodiola rosea* extract and SSRI medication, I have not observed any untoward interaction when patients take them concomitantly during the tapering process. Therefore, it is important to inform all patients of this possibility and instruct them to contact you immediately should they experience a sudden onset of heart palpitations and increased heart rate.