Melatonin: Route of Administration

Melatonin, as a supplement, is most often used through the oral route. There are a number of excellent reviews that deal with the time to maximum blood levels, dosages and biavailability[1, 2]. In general, research shows that after taking oral immediate-release formulations of melatonin, maximum blood levels may be reached after 45-50 min. It is clear that major variations can occur, related to inter-individual differences in drug absorption, distribution, metabolism, and elimination. It is also important that these studies show that the bioavailability is generally low (~10-15 %), with a significant intra-individual variability. This percentage may be misleading, since there are many different release formulations, with slow-release forms having a much higher bioavailability.

Alternate pathways for administration are available[3]. Both rectally and vaginally administered melatonin may serve as alternatives to standard oral melatonin therapy. In addition, transdermal delivery of melatonin is used on occasion, when prolonged effects are intended. Melatonin administered by these routes of administration was safe.

In the case of the rectally administered route, there is a more limited history. When administered through this route, melatonin is absorbed through two different vascular systems, one of which delivers it to the liver while the second bypasses the liver. Rectally administered melatonin is usually advertised for its powerful antioxidant effects. However, this message is often combined with its effect as a 'sleep aid'. The dosages are very high, often advertised as upwards of 200 mg. A further selling point, mentioned for most suppositories, is the inherent fact that this route avoids degradation in the GI Tract, allowing for greater bioavailability. In addition, these suppositories are mostly sold in slow-release forms. All of this true and often very advantageous for administration and personal needs.

What must be kept in mind, however, is that levels of melatonin in the blood are normally measured in the low **PICOGRAM** range. It, therefore, begs the question as to where all this melatonin is going, how the high levels are affecting endogenously produce melatonin, overdosing, the reliability of the adjunctive materials in the suppository that guarantee reliable slow release, etc.
My research of the literature did not find good in-depth discussion of these issues. I would therefore suggest that, although in general suppository forms of administration of drugs has a long history of efficacy, one should do more critical assessment of this modality of use for melatonin prior to use.

Reference:

1. Harpsøe NG et al. Clinical pharmacokinetics of melatonin: a systematic review. Eur J Clin Pharmacol 2015; 71: 901-909.
2. DeMuro RL et al. The absolute bioavailability of oral melatonin. J Clin Pharmacol 2000; 40: 781-784.
3. Zetner D et al. Pharmacokinetics and Safety of Intravenous, Intravesical, Rectal, Transdermal, and Vaginal Melatonin in Healthy Female Volunteers: A Cross-Over Study. Pharmacology 2021; 106: 169–176.