Clinical Review:

Suppositories

Suppositories are one of the mainstays of the pharmaceutical compounding industry. Rectal delivery of medication is essential for patients who cannot tolerate oral medication or are unable to take it, such as those on hospice care, pediatric patients, or patients with seizure disorders. They are also often used for delivery of medications locally for conditions in which systemic use may carry unnecessary risk or the treatment cannot reach the site of action at appropriate levels. Some examples include cases of formulations for vaginal dryness or hemorrhoids. Suppositories are most commonly used rectally or vaginally, though urethral suppositories can be compounded as well.

Not all active ingredients can be well absorbed rectally or vaginally. Generally, before taking on a preparation, it is best to review existing literature to see if there is data on systemic absorption from rectal routes, and if so, how well it is absorbed. For example, data exists to suggest that ibuprofen can be absorbed through rectal routes but with approximately 60% of the bioavailability of oral use.1 Alternatively, systemic exposure from rectal lidocaine is approximately twice that compared to the same dose taken orally due to the fact that rectal administration bypasses hepatic metabolism.2 If literature is unavailable, review the drug characteristics to determine if it can be absorbed rectally adequately. Generally, drugs with lipophilic characteristics, relatively low molecular weight, and that are not in an ionized state have a better chance of absorption through the rectal mucosa.3 Because the rectum has a relatively neutral pH, drugs with a pKa near or above physiologic range will be more readily absorbed, as they will not be ionized in the rectal fluid, making them more lipophilic.3

After determining if the API can be used rectally, it is time to select the appropriate base. Generally, there are two types of bases available: fatty type bases and PEG type bases. Fatty type bases include Witepsol, Cocoa Butter, and various other combinations of hard fat derived from palm kernel oil and coconut oil. Cocoa Butter has a lower melting point of approximately 34C, and other fatty-type bases derived from palm kernel oil typically melt at 35-37C. PEG bases are often composed of high and low molecular weight PEG and melt at slightly higher temperatures. Though melting does play a role in the release from PEG suppositories, one of the main mechanisms of delivery is dissolution in the rectal fluid.3,5 This means PEG suppositories generally have longer residence time than fatty suppositories. The relative lipophilicity of the base can determine which base that you select.

The general rule is:
Lipophilic API in PEG base -> moderate release rate
Hydrophilic API in PEG base -> moderate release rate
Lipophilic API in Fatty base -> very slow release
Hydrophilic API in Fatty base -> rapid release

For example, when compounding rectal diazepam, the rate of release can be very important. Diazepam has lipophilic qualities, so per the above chart, a PEG base should have faster release. Comparative studies of the release rate of diazepam in fatty bases vs hydrophilic bases confirm this.5 Generally, lipophilic APIs paired in PEG bases and hydrophilic APIs in fatty bases have the fastest release profiles.

After the base has been selected, determining the suppository mold size is next. Mold size selection can depend on age and route. Generally, 1mL suppositories are often used in pediatric patients, while a 2mL mold size is most common for vaginal and rectal use in adults. The amount of powder that will be added must also be taken into account. There is no hard and fast rule, but generally, the amount of powder added should represent approximately 1/3 w/v or less of the suppository. Higher powder volumes can result in brittle suppositories or in significant changes in melting point, which can, in turn, affect drug delivery.

For more information on the formulation of suppositories, become a Fagron Academy Compounding Technical Support (FACTS) member and check out our how-to video on compounding and heat-sealing suppositories. FACTS members have access to live formulation help as well as our formula database with a myriad of suppository formulations.

Sources:

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