

FORMULATING PEDIATRIC TASTE MASKED MULTIPARTICULATES USING CPS® TECHNOLOGY

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INTRODUCTION

Developing formulations appropriate for children still remains to be a major formulation challenge for the pharmaceutical scientists as children are different than adults in many aspects of pharmacotherapy, including capabilities for drug administration, medicine-related toxicity, and taste preferences. The administration of drug, dosage accuracy, toxicity, and taste must be taken into consideration for the appropriate usage of the drug as well as the compliance and adherence to the treatment.

Currently many pediatric medicinal needs are unmet as the available adult formulations are not suitable for administration to children. Besides, development of multiple dosage forms for different age groups will rarely be commercially viable and liquid formulations, which can be given to a broad age group, however, would present particular challenges, for example masking the bitter-taste of drug and maintaining its stability throughout the shelf-life of the product. Dosage forms like orodispersible or chewable preparations are being used but carry a significant risks of choking and chewing.

Recently, mini-tablet is gaining growing interest as a promising dosage form for pediatric population. However, due to their small size, minitables may not be appropriate for patients with motor impairment or geriatric patients, unless administered by a caregiver or a dosing device. Difficulties may also be encountered when designing a minitabled-based dosage form for high-dose drugs (compounds with low potency), since the number of minitables per dose can be prohibitively large along with the labor-intensive manufacturing can lead to much higher production costs.

Multiparticulates are well understood dosage forms that provide a very high level of dose flexibility and can be developed to meet specific requirements of pediatric and geriatric age groups. This dosage form and its processing have a long been studied and well received and as such provide development flexibility like no others. Besides, multiparticulates can also be the choice of formulation to avoid stability issues commonly associated with liquid formulations.

The sub-millimeter size of these multiparticulate sub-units offer 1) dose flexibility; 2) can be administered through capsules, sprinkle capsules, sachets, stick packs, straws; and 3) their small size makes them most convenience for oral administration to both the pediatric and geriatric population as they often experience troubles swallowing. Many times, the modification from the adult dosage form only requires a capsule fill adjustment. Therefore, multiparticulates is a dosage form that meets a wide range of formulation requirements for the pediatric population.

PURPOSE

To develop a multiparticulate (drug pellets) formulation appropriate for oral administration for a wide pediatric age range using Glatt's CPS® technology, taste mask the CPS drug pellets using a taste masking (TM) polymer and thus enhance the palatability and patient compliance. The multiparticulate dosage form is designed to release immediately in the gastrointestinal tract to maximize absorption of the drug upon swallowing.

METHODS

The pellets were produced by direct pelletization method using the CPS® technology in GPCG 1.1 with CPS-3 insert. The formulation consisted of Active Pharmaceutical Ingredient (API), a disintegrant and microcrystalline cellulose. Several batches of CPS pellets were produced and screened to obtain desired pellet size of 200-350 micron. CPS pellets were then coated at different weight gains with taste masking polymer (Eudragit EPO). Pellet surface morphology was evaluated using Scanning Electron Microscopy (SEM). Pellets were analyzed for drug assay, water content by Karl Fisher and dissolution to evaluate the taste masking performance.

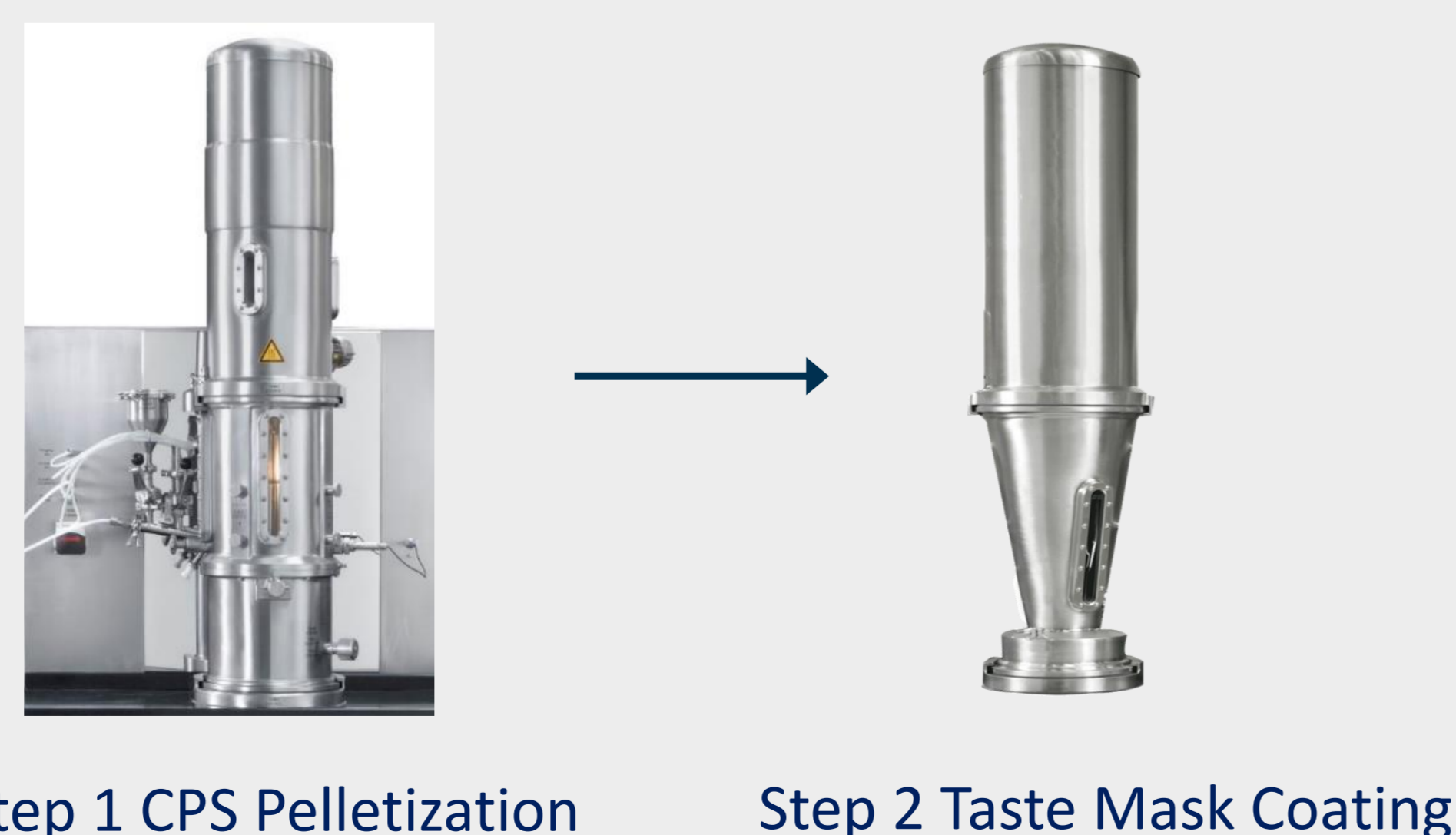


Figure 1: Process Flow Diagram

RESULTS

The CPS drug pellets produced were spherical in shape with smooth surface morphology (Figure 3). The pellets were dense with bulk density of ~0.7 g/ml and narrow particle size distribution. Each CPS batch yielded over 80% of the target pellet size range of 200-350 micron, which is suitable for pleasing mouth feel for both pediatric and geriatric populations. The drug assay of the taste masked pellets were between 98.9 to 100.5%. The water content by Karl Fisher ranged between 1.4 -1.6%. The dissolution profile (Figure 4) showed no drug release at pH 6.8 (oral cavity) suggesting successful taste masking coating and more than 95% of drug released in 30 minutes in acidic pH (representing stomach). No significant difference was observed between different taste masked coating levels.

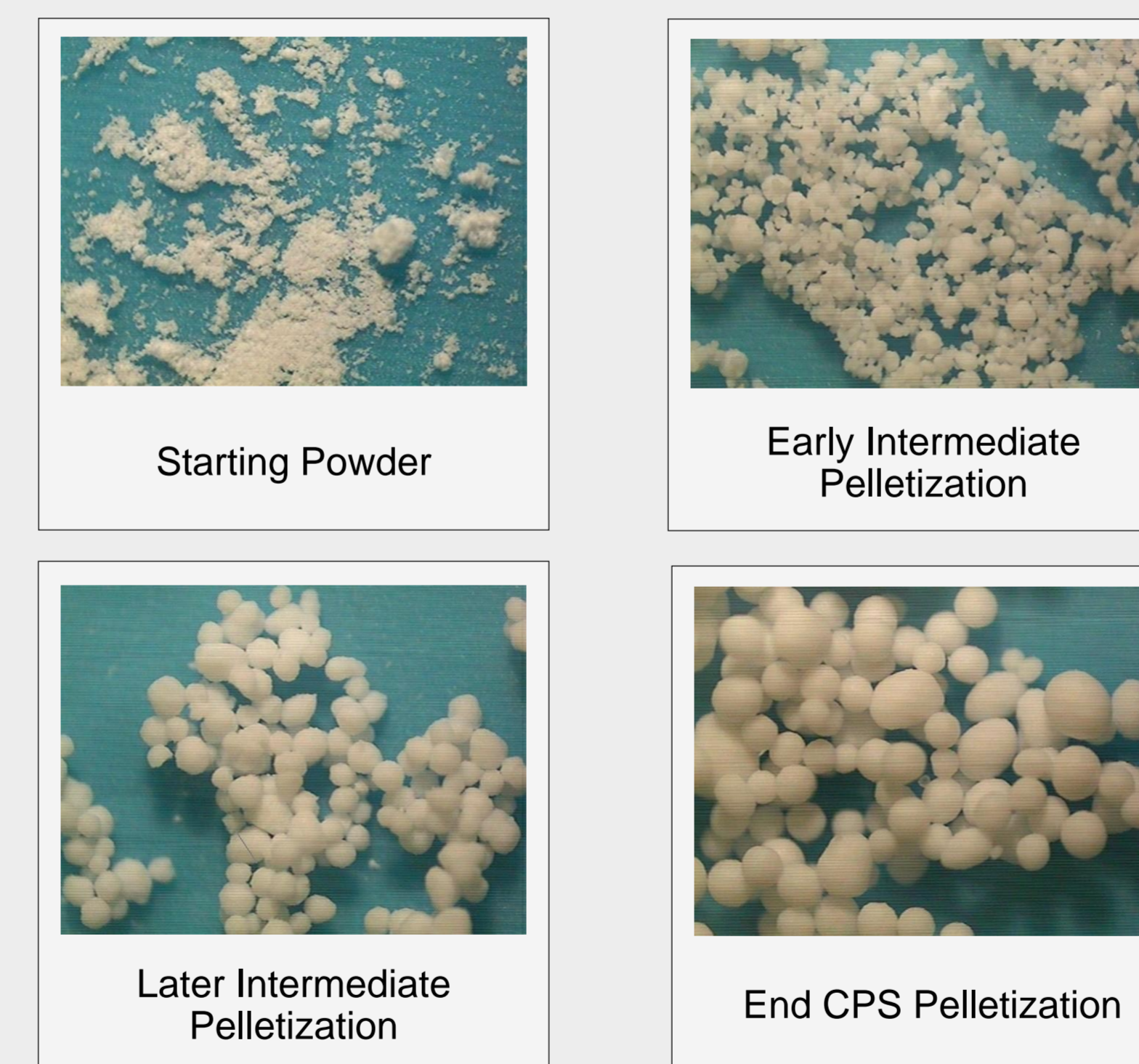


Figure 2: CPS Direct Pelletization Process

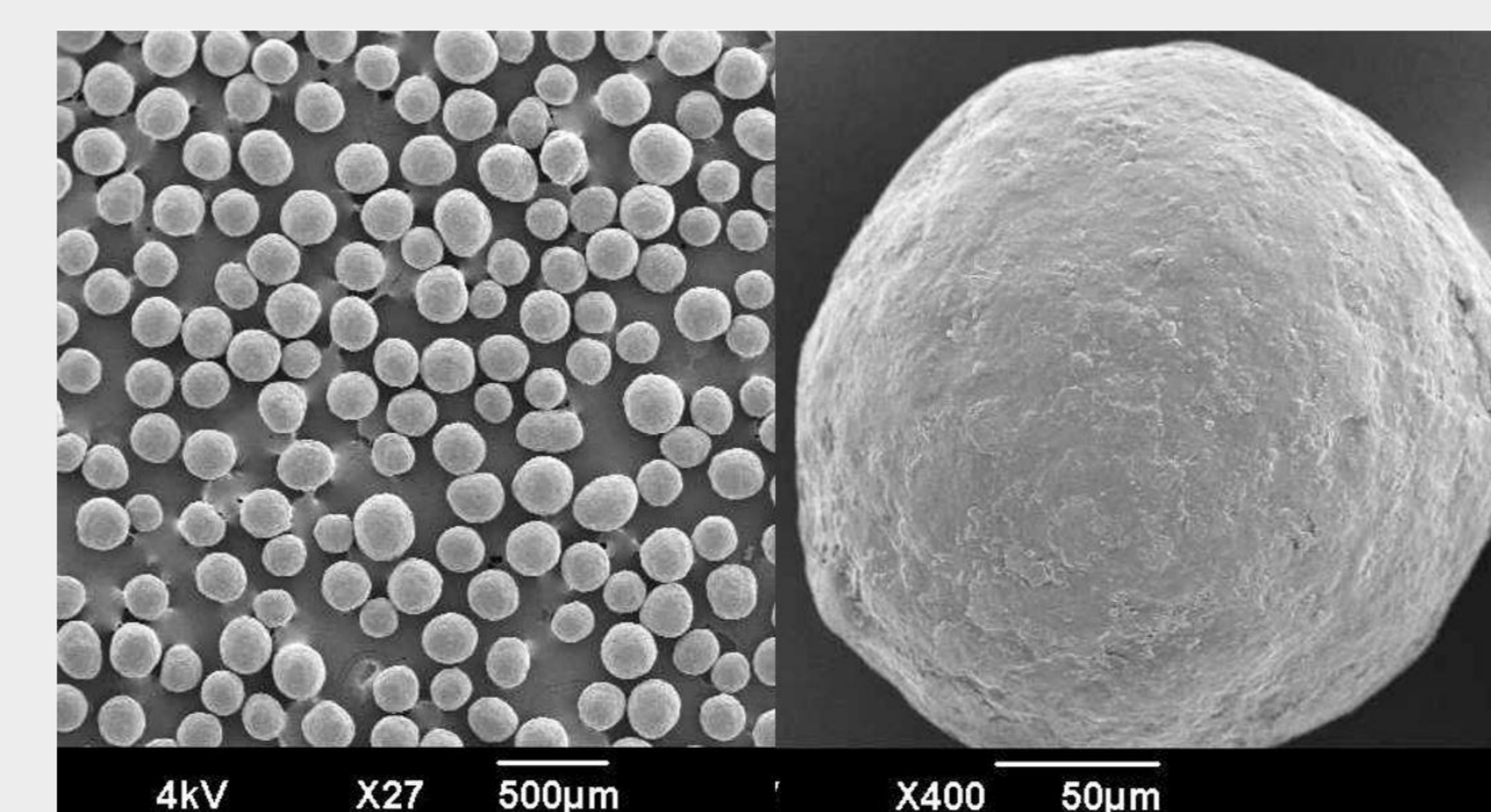


Figure 3: SEM of Taste Masked CPS Multiparticulates

CONCLUSION(S)

The study confirmed that multiparticulates produced by Glatt's patented CPS® technology were suitable for subsequent taste mask coating due to their spherical shape, smooth surface, high bulk density and narrow particle size distribution. Once coated, the pellets were effectively taste masked as shown by no drug release in pH 6.8 (oral cavity) and immediate drug release in acidic pH (stomach). In conclusion, a successful formulation of taste masked CPS pellets was developed for both pediatric and geriatric population.

CPS pellets can be used for a wide pediatric age group as well geriatric population due to their small particle size as they provide a pleasant mouth feel. Additionally, due to the long and extensive knowledge, multiparticulates can be used as one of the best formulation platforms for most drugs for both pediatric and geriatric populations.

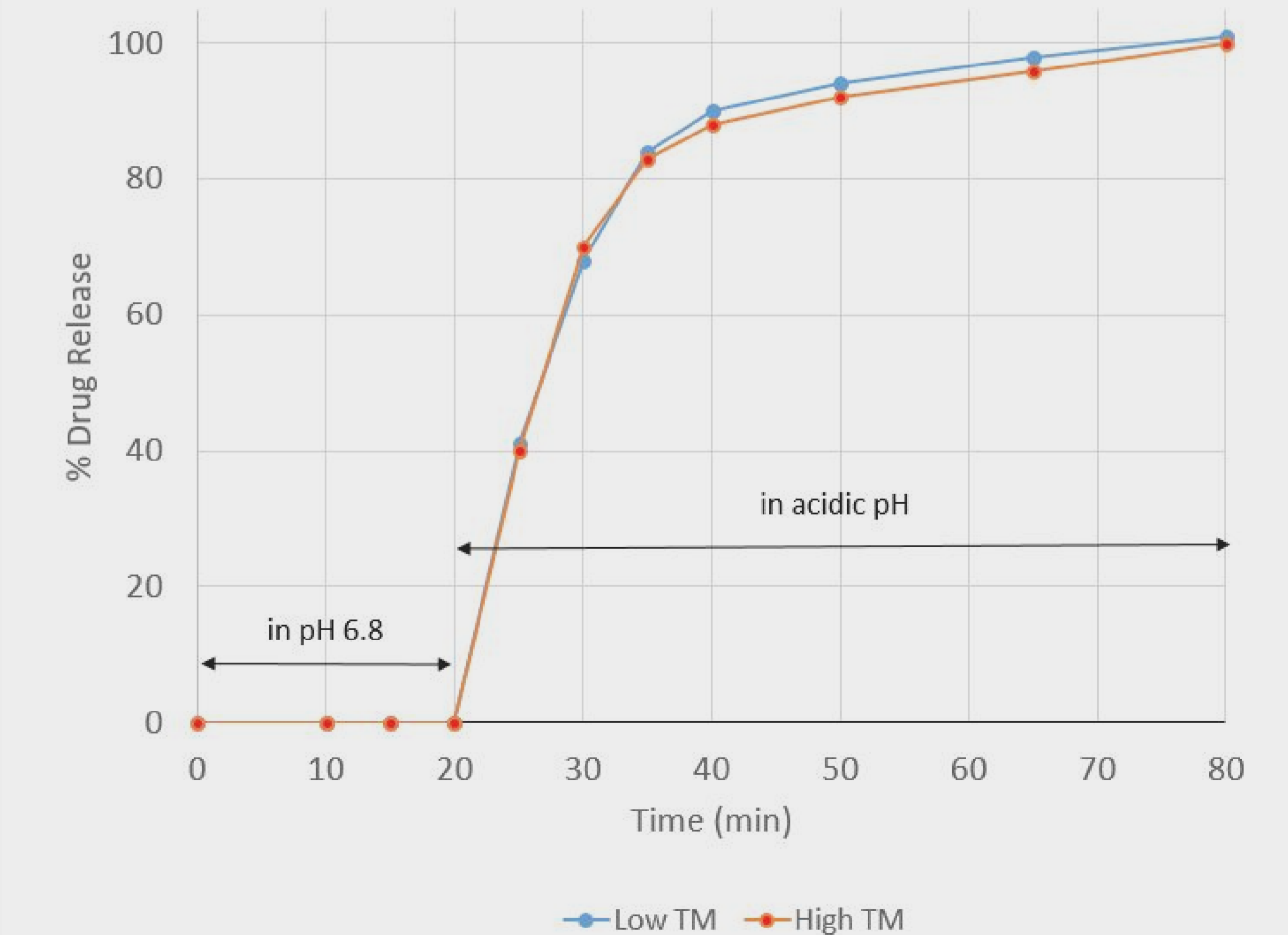


Figure 4: Dissolution Profile of Taste Masked CPS Multiparticulates

