Influence of Adsorption during Grinding on the Analytical Quantification of Active Ingredients in Medicinal Products

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Introduction

Sample preparation is a major process in analysis, consisting of the necessary operations needed to modify the sample for subsequent delivery of the analytes in a convenient form for analysis. Despite the fact that the proper execution of sample preparation is paramount in achieving accurate quantitation, it is generally not the focus of attention in discussing pharmaceutical analytical methods [1]. Grinding is common practice to reduce particle size and homogenize the sample; however, when under physical contact with the interface, particles are subject to a number of interactions. Forces such as van der Waals forces, electrostatic forces, and valency forces at the surface, which are normally insignificant, become prominent during grinding, and may be sufficient to cause adsorption of molecules at the surface of a particle. The objective of this study was to investigate the influence of adsorption of active pharmaceutical ingredients during grinding of tablets for assay testing of drug products. It was investigated whether ceramic, glass and stainless steel surfaces, each represented by a pestle and mortar, influenced the assay values of simvastatin, alendronate sodium and perindopril erbumine active ingredients.

Methodology

For each drug product and grinding surface, a recovery study was first carried out to show accuracy and reproducibility of the method chosen for residue quantification, namely the rinsing method. This involved spiking the surfaces with a known amount of active ingredient at three levels corresponding to 2.5%, 5.0% and 7.5% with respect to the theoretical amount of active present in each pestle and mortar for each grind, followed by a rinse recovery.

Tablets of the three drug products were assayed and any active residue on the pestles and mortars following grinding was recovered and quantified. The given assay procedure for each drug product was carried out under the following conditions:

a) Dissolution of whole tablets
b) Tablets ground with a ceramic pestle and mortar
c) Tablets ground with a glass pestle and mortar
d) Tablets ground with a stainless steel pestle and mortar

The samples were analyzed for the active ingredient by HPLC using the assay test method of the bulk finished product methods, developed and validated by Arrow Pharm (Malta) Ltd. The percentage assay of active in each of the sample solutions was calculated and the values obtained for the different grinding surfaces were compared to each other and to that of dissolution of whole tablets.

Chemical Structures

Figure 1: Simvastatin

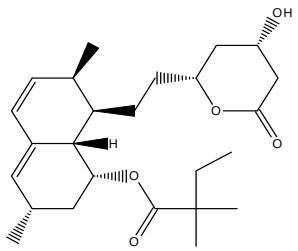


Figure 2: Perindopril

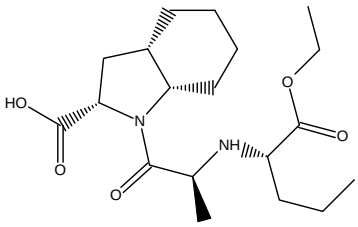
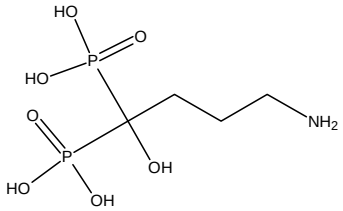


Figure 3: Alendronate



Results

Figure 4: Mean percentage recovery of active after spiking.

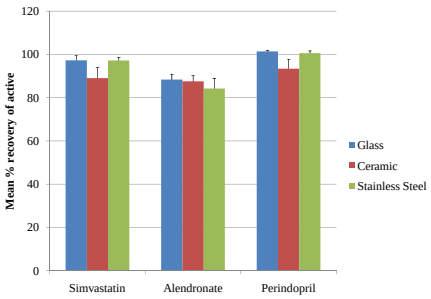


Figure 5: Mean percentage assay of active for the assay of tablets.

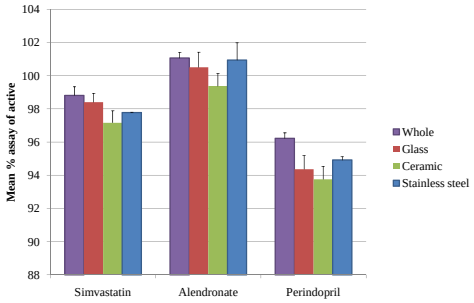
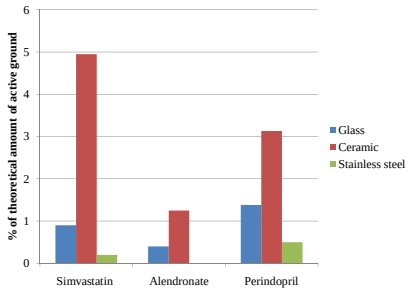


Figure 6: Residue recovered after grinding as percentage of the theoretical amount of active ground.



Conclusions

The results obtained indicate that the three drug products were effectively influenced by grinding, resulting in a decrease in their percentage assay values when compared to the absence of grinding. Surface interactions, such as van der Waals forces, leading to the adsorption of molecules may be responsible for the loss in percentage assays that were experienced. The extent to which the different actives were influenced may be attributed to the different physicochemical properties of the drugs. Analyses confirmed that ceramic was the most distinguished material, while perindopril differed mostly from simvastatin and alendronate in terms of the extent to which they were influenced by grinding. The significant difference between ceramic and the other two surfaces may mostly be due to the greater surface roughness of ceramic compared to that of glass and stainless steel; hence active may be retained more easily. The increased influence adsorption had on perindopril was attributed to the polyfunctional nature of the molecule through which a variety of bonding interactions may take place. Furthermore, the molecular structure is such that all the functional groups are well exposed and thus very likely to interact with the grinding surface, leading to adsorption. On the other hand, the molecular properties of simvastatin and alendronate are such that fewer types of possible interactions with the grinding surface are envisaged.

References

1. Choi, C.K.; Dong, M.W. Sample Preparation for HPLC Analysis of Drug Products. In *Handbook of Pharmaceutical Analysis by HPLC;* Ahuja S. and Dong, M.W., Eds.; Elsevier, 2005; p 123-144.