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Letter to Editor

The Polymorphism Effect in Active Pharmaceutical Ingredients (API): A Issue Affecting on Bioavailability And Bioequivalence of Drugs

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The chemical and physical properties of the active pharmaceutical ingredients (API) on solid-state form can be affected by polymorphism effect. This effect can have a significant influence on the apparent solubility of the drug substance. Polymorphic forms of API differ in their internal solid-state structure, these compounds show a different crystallographic arrangements and different H-bonds self-arrangements [1,2]. The consequences of this effect in a drug substance which may exists in various polymorphic forms are change aqueous solubilities and dissolution rates [3].

The "Guidance for Industry, ANDAs: Pharmaceutical Solid Polymorphism" recommend the control and study of this theme. For FDA the control of polymorphism in drugs is required and is a condition for security sanitary, in order to ensure the best therapeutic efficacy of the drug. According to FDA when a specific polymorphic form shows differences in apparent solubilities, the focus of the research should be on the potential effect such differences have on drug bioavailability and bioequivalence.

Drugs contaminated with polymorphic forms can have low water solubility and are predisposed to poor and variable oral bioavailability, and consequently can affect clinical responses [4].

Therefore, "Bioavailability (BA) is defined in 21 CFR 320.1(a) as: the rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action; Bioequivalence (BE) is defined in 21 CFR 320.1(e) as: the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study."

Therefore, under normal conditions, without effects of polymorphism, the drugs are in accordance with the criteria defined above. When an API responds positively to the bioavailability and bioequivalence criteria, we can infer positive aspects for its use in a drug, and consequently we can expect a good clinical efficiency of this drug.

According to Silva et al. [5], in the last years, the crystallographic aspects and their consequences around polymorphism effects have been the focus of several books. For the pharmaceutical industry, the main concern are the effects of the appearance of unwanted polymorphs within the active pharmaceutical ingredients, formulations, and tablets, a problem that can appear throughout the production chain and therefore must be very well monitored.

The first step to achieve a full research on polymorphic forms is through their complete characterization, and this can be done by different analytical techniques to investigate structural properties, such as single crystal X- ray diffraction (SCXRD) and polycrystal X-ray diffraction (PXRD), solid-state nuclear magnetic resonance (solid-state NMR), and infrared spectroscopy (IR). The second step is to test the bioavailability and bioequivalence these polymorphs.

Therefore, when conducting a complete study of polymorphic forms on API, the information and data obtained in this research can help to develop more reliable drugs.

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References

1. Raw AS, Furness MS, Gill DS, Adams RC, Holcombe J FO, et al. (2004) Regulatory considerations of pharmaceutical solid polymorphism in abbreviated new drug applications (ANDAs). Adv Drug Deliv Rev 56(3): 397-414.

2. Vippagunta SR, Brittain HG, David JW, Grant DJW (2001) Crystalline solids. Adv Drug Deliv Rev 48: 3-26.

3. Brittain HG & Grant DJW (1999) Effect of polymorphism and solid-state solvation on solubility and dissolution rate. In: HG Brittain (eds.), Poly-

morphism in Pharmaceutical Solids. Marcel Dekker, New York, USA, pp. 279-330.

4. Censi R & Martino PD (2015) Polymorph impact on the bioavailability and stability of poorly soluble drugs. Molecules 20(10: 18759-18776.

5. Silva RP, Ambrósio MFS, Piovesan LA, Freitas MCR Marques de ADL, et al. (2018) new polymorph form of dexamethasone acetate. Journal of Pharmaceutical Sciences 107(2): 672-681.