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Zeolite-rich powder as bio-active carrier for amoxicillin oral delivery: a preliminary study.

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Amoxicillin is an antibiotic often employed to treat gastric infections. Some of these develop in sites where a pH alteration took place, then possibly enhanced by the infection itself. Due to its properties, the zeolite clinoptilolite has been already successfully used to regulate the pH in the stomach. A research program aimed to evaluate clinoptilolite as carrier for amoxicillin has begun, to investigate if a synergic action of the two components, carrier and drug, can be obtained. This preliminary study has covered the following aspects:
- characterization of the rock selected;
- preparation of a clinoptilolite-rich powder;
- preparation of ten batches of material micronized using different parameters (solid mass, liquid volume, milling time);
- determination of particle size and particle distribution;
- study the technological properties of materials useful for pharmaceutical applications such as true and bulk densities and flow properties according to European Pharmacopoeia VII ed.
Furthermore, amoxicillin stability tests in simulated biological fluids at different pHs (1.2, 4.0 and 6.8) and temperatures (4, 20 and 37°C) have been performed.
A clinoptilolite-rich Sardinian epiclastite, Oligo-Aquitanian in age, has been subjected to chemical (ICP) and mineralogical analyses (XRPD analysis, Rietveld method, Topas software). A zeolite-rich powder has been prepared by autogenous comminution and dry sieving, obtaining a material finer than 150μm with about 80% of zeolite content. This material has been micronized with a McCrone mill; then each batch has been analyzed by Laser diffraction to measure the effects of the different micronization parameters on size and size distribution of the materials. Narrow leptokurtic curves, right skewed, and mode values of 5.35 and 4.44μm, are obtained with solid-to-liquid ratio of 0.25 and 0.33 g/ml, respectively, by milling 4 g of zeolite-rich material for 10 minutes. Furthermore, grinding enhances zeolite delamination according (010) plane, that presents a perfect cleavage and the widest surface among clinoptilolite's planes. Consequently, on the XRD patterns of micronized powders the intensity of (010) peak increases with milling efficiency, whereas the reflections of the other zeolite planes do not show significant variations. By increasing the specific surface of the material, the delamination should be an advantage in view of the planned drug loading.
The true density of all samples is 2.2 g/cm3; bulk and tapped densities are comprised between 0.4-0.5 and 0.6-0.7 g/cm3, respectively. All micronized materials demonstrate poor flow properties, as foreseeable because of the hydrophilic nature of the zeolite. Powders with wide particle size distribution show compressibility indexes in the range of 25-40%, which are better than well sorted powders.
Amoxicillin trihydrate proves to be stable in simulated biological fluids at pH 4.0 and 6.8 regardless temperatures tested. On the contrary, at pH 1.2 drug stability is temperature dependent as degradation of about 30% is observed at 37°C after 3 h; however, this period is longer than the usual gastric emptying time.