



# DRUG-DRUG COCRYSTALS FOR THE TREATMENT OF HYPERTENSE DIABETIC PATIENTS

Patent Application Number: MX/a /2017/013510  
(Status: patent pending)



## ABSTRACT

This invention presents the synthesis process and characterization of cocrystals which incorporate two APIs (Metformin hydrochloride in presence of a thiazide) through mechano-chemical methods for its application on the treatment of diabetic patients (DMT2) who also present hypertension problems.

## BACKGROUND

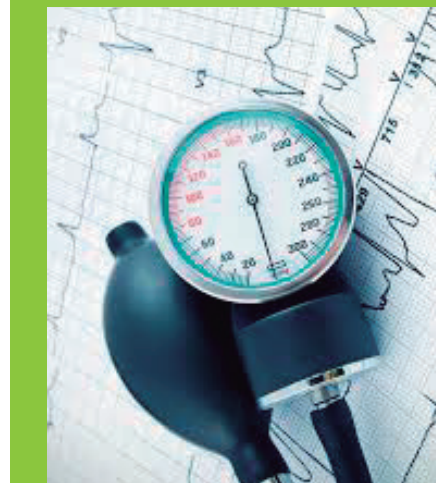
Pharmaceutical cocrystal are multicomponent crystals formed by an active pharmaceutical ingredient (API) and a coformer (crystallizing agent which is embedded in the crystalline structure of the API), both API/coformer are present in defined proportions. However, the preparation of drug-drug cocrystals (API/API) has been developed, in which in the same crystalline phase, the coformer is substituted by another API, forming a cocrystal where both therapeutic effects are present.

## STAGE OF RESEARCH

In this moment, the development lies as a proof of concept, thus both the design and synthesis of drug-drug cocrystals has been performed. This cocrystals have the general formula  $[MET \cdot HCl][TZ]$  containing metformin hydrochloride in presence of two different thiazides (chlorothiazide (CTZ) and hydrochlorothiazide (HTZ)) and were obtained through mechanochemical methods which use the minimum amount of solvent needed. Solid phases have been characterized by different spectroscopic techniques, X-ray diffraction, differential scanning calorimetry and thermogravimetric analysis methods. Currently the cocrystal is formulated as a solid pharmaceutical form for its use in a preclinical protocol of safety and efficacy.

## DESCRIPTION

This invention presents the synthesis process and characterization of cocrystals which incorporate two APIs (Metformin hydrochloride in presence of a thiazide) through mechano-chemical methods for its application on the treatment of diabetic patients (DMT2) who also present hypertension problems.



## APPLICATIONS FIELD

The suffering of both DMT2 and hypertension in a patient potentially increase their cardiovascular risks. Therefore, the prevention of complications in patients with diabetes must have a multifactorial approach. Administering several drugs at the same time may improve therapy in complicated illnesses that need multiple medicines. In this specific case, this property is exploited for the treatment of patients presenting both comorbidities: diabetes (type 2) and hypertense problems which are common in Mexico.



## ADVANTAGES

The cocrystals from this development [MET•HCL][TZ] containing metformin hydrochloride in presence of chlorothiazide (CTZ) or hydrochlorothiazide (HTZ) have potential benefits in their production methods and may supply different kinds of synergisms compared to the administration of the individual APIs. This may represent a potential application in the treatment of diabetic patients (DMT2) with hypertension, the simplification of the treatment, the

improvement of clinical results, and the prevention of further expenses due to the progression of the illnesses, such as cardiovascular problems.

No solvent reactions (or the minimal use of solvents in a reaction) allow for a decrease on the pharmaceutical manufacturing costs, modification to intrinsic solubility of the employs APIs, thermal stability, solution kinetics, bioavailability – crucial in pharmaceutical techniques for the formulation of new pharmaceutical alternatives in the treatment of chronic diseases – decrease in the required therapeutic doses, increase in therapeutic and clinical effects, an important decrease in drug resistance, and different kinds of synergisms compared to the administration of the individual APIs represent some of the main competitive advantages of this development.