A new Pharmaceutical Preparation Comprising Metformin, Vitamin B_1, Vitamin B_6, Vitamin B_{12} and Folic acid as an Oral Tablet Dosage Form.

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Abstract

A new Pharmaceutical Preparation Comprising Metformin, Vitamin B_1, Vitamin B_6, Vitamin B_{12} and Folic acid as an Oral Tablet dosage form.

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Metformin is a well-known oral hypoglycemic agent used to control Type 2 Diabetes mellitus, it is also known to cause deficiency of vitamin B12 & Folic acid due to interference with their absorption orally. Prolonged administration of metformin causes an elevation in the level of plasma homocysteine which is now known to be correlated with a wide array of illnesses.

The aim of this study was the preparation and optimization of a new pharmaceutical combination comprising metformin, vitamin B_{12}, B_6, B_1 and folic acid as immediate release oral tablets for management of Type 2 Diabetes mellitus and aims to decrease level of plasma homocysteine associated with Diabetes mellitus and long term use of metformin. Then, evaluation of the prepared tablets in terms of physical characterization and drug release according to USP standards. For that, a method of analysis of the five active ingredients was to be developed and validated using tandem mass spectroscopy. Compatibility of API(s) was tested by Deferential Scanning Calorimetry (DSC). Also, their stability in solution was investigated.

Metformin and the 4 vitamins (vitamin B1, B6, B12 and Folic acid) were prepared as immediate release tablets and coated with Sheff Coat ^{TM}. The prepared tablets were evaluated for physical characteristics according to the standards of the USP quality control tests of the immediate release tablets (USP 2009).The physical characteristics that were evaluated were: weight variation, hardness, friability test and disintegration. The drug(s) release was evaluated by dissolution test

using type II dissolution apparatus. Assay method was developed for this novel formula to evaluate this combination formulation, also validation of this method was done using tandem mass spectroscopy which is a highly sensitive method and it was chosen for this project due to the fact that the formula contains 5 API(s). The method was developed and validated according to European Pharmacopeia (EP) using LC MS/MS.

The results show compatibility of the active materials. The tablet evaluation in terms of physical characteristics and drug release were all within the USP standards where more than 75% of all active ingredients were released in less than 45 minutes. Also there was no significant differences in drug release between coated and uncoated tablets taking $T_{30\%}$ as a comparison point.

The assay method was developed successfully and the validation parameters were all within the limits stated by European Pharmacopeia which demands that the relative standard deviation (RSD) should be less than 2% for each parameter. System suitability gave RSD between 0.128 and 1.366 for all ingredients; repeatability gave RSD between 0.177 and 1.884, intra-day precision was 0.105-1.72, interday precision was 0.084-1.519. Linearity were achieved for the five active ingredients and the correlation coefficient exceeded 0.99. Assay of tablet content gave 97.5 - 102.0% of all ingredients with RSD<2%.

In conclusion, the suggested formula was successfully put in a design of orally administered immediate release tablets and the method of assay was successfully developed and validated.

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