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COMPATIBILITY TESTING OF GUAR GUM WITH METFORMIN HYDROCHLORIDE

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ABSTRACT

Guar gum has gained immense importance because of its constructive role of releasing sugars and absorbing sugars slowly in the intestinal tract; consequently, reduce the severity of diabetes mellitus and also act as a prospective hydrophilic matrix carrier for oral controlled delivery of drugs. Metformin hydrochloride is an oral antidiabetic drug and first-line drug of choice for the treatment of type 2 diabetes, in particular, in overweight and obese people. In this study, an approach to possible physical interaction between metformin hydrochloride and guar gum is presented. For the investigative purpose; molecular level property, particulate level property and thermal methods of analysis have been assessed. Results of FTIR, PXRD and DSC studies indicated that Guar gum had compatibility with Metformin hydrochloride

Key words: Metformin hydrochloride; guar gum; molecular level property; particulate level property; thermal methods of analysis.

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INTRODUCTION

Metformin hydrochloride is an oral antidiabetic drug and first-line drug of choice for the treatment of type 2 diabetes, in particular, in overweight and obese people. Metformin works by suppressing glucose production by the liver.Dietary fiber has established benefits for health maintenance, disease prevention, and as a component of medical nutrition therapy. It consists of the storage and cell wall polysaccharides of plants that cannot be hydrolyzed by human digestive enzymes. Consumption of viscous dietary fibers lowers blood cholesterol levels and helps to normalize blood glucose and insulin levels. Reflecting the recent health boom, there is increasing use of a variety of health foods by a wide range of age-groups across the world. Some dietary fibers' like guar gum and pectin are known to exert pharmacological activities i.e. to lower blood sugar levels. In recent years, considerable attention has been focused on hydrophilic polysaccharides in the design of oral controlled drug delivery systems because of their flexibility to obtain a desirable drug release profile, cost-effectiveness and broad regulatory acceptance[1, 2,3,4,5]. Guar gum is a prospective hydrophilic matrix carrier for oral controlled delivery of drugs with varying solubility and therefore many reports have been published on the use of guar gum for oral delivery of drugs .Guar gum is a water soluble polysaccharide derived from the seeds of *Cyamopsis tetragonolobus*, family Leguminosae. In pharmaceutical formulations, GG is used as a binder, disintegrant, suspending agent, thickening agent and stabilizing agent. GG is soluble in cold water, hydrating quickly to produce viscous pseudo plastic solutions that although shear thinning generally have greater low-shear viscosity than other hydrocolloids .This gelling property retards release of the drug from the dosage form[6]. Assessment of possible incompatibility between an active drug substance and excipient is an important part of the development of the dosage form of a drug. The essence of compatibility tests is to mix samples of the active substance with the excipients and to study the mixtures stability[7, 8, 9,10].In this study, as an approach to possible physical interaction between metformin hydrochloride and guar gum is presented. For the investigative purpose; molecular level property, particulate level property and thermal methods of analysis have been assessed. These preliminary studies were performed since we intend to prepare a multiparticulate delivery system for metformin hydrochloride using natural polymer viz. guar gum.

MATERIALS AND METHODS

Materials: Metformin Hydrochloride (Drug) and Guar gum (Polymer) were provided as gift samples from Akumbs Pharmaceuticals Ltd. Rorkee, India and Dinesh Enterprises, Jodhpur, India respectively. Drug-polymer samples were prepared as a 1:1 (w/w) mixture by blending and co-grinding. Samples of individual components as well as drug-polymer physical mixture were subjected to FTIR, powder X-ray diffraction and DSC studies.

Methods

Fourier Transform infrared (FTIR) spectroscopy

The KBr disk sample preparation technique was used to obtain the IR spectra of the samples on an IR spectrophotometer (Shimazdu-FTIR-8400S.). The scanning range was selected between 4000 and 400 cm^{-1}.

Powder X-ray diffraction (PXRD)

X-ray diffraction was performed on 18 KW Cu rotating anode based powder diffractometer fitted with curved crystal monochromator in the diffracted beam (Rigaku). The x-ray generator was operated at 40 kV and 100 mA. Samples were placed on a quartz sample holder at room temperature and were scanned at diffraction angle 2θ from 5° to 100° at the scanning rate of 3°/ min.

Differential Scanning Calorimetry (DSC)

DSC measurements were carried out using Mettler-Toledo (Model -823) DSC under nitrogen atmosphere. The samples were heated from 30 to 300°C at a scan rate of 10 °C/min. The peak temperature and enthalpy of fusion were measured from the endotherm using a computer attached to the instrument. The DSC was calibrated with indium and zinc before use.

RESULTS AND DISCUSSION

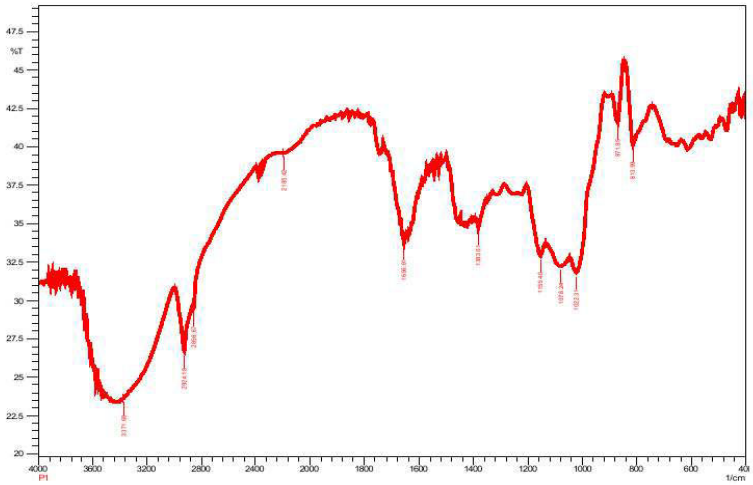
Fourier Transform infrared (FTIR) spectroscopy

FTIR spectra of Metformin hydrochloride reported characteristics bands of N-H stretching, N-H deformation, N-H bending, C=N stretching, C-N stretching and C-H deformation at 3298.38, 1568, 798.56 & 734.90, 1627.97, 1166.97 and 1475.59 respectively as shown in Table 1. All the characteristic peaks of Metformin hydrochloride were observed in the physical mixture without any changes in band assignments (Figure 1).

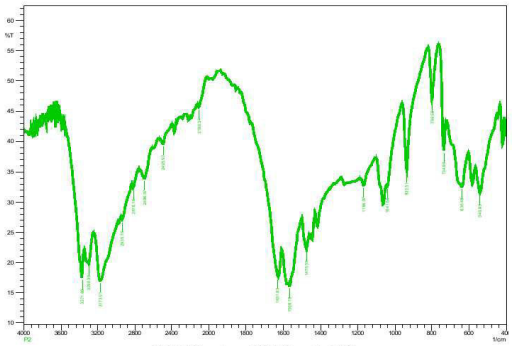
Table 1
FT-IR Studies of Metformin HCl, Guar gum and Physical Mixture

Frequency range (cm-1)	Observed frequency (cm^{-1})			Band Assignment
	Metformin HCl	Guar Gum	Physical Mixture	
3400-3100	3298.38	3371	3371.86 3298.38	N-H stretching
1590-1530	1568	3371	1573	N-H deformation
910-660	798.56 734.90	871.85 813.99	869.92 798.56	N-H bending
1685-1580	1627.97	1656.91	1629.09 1654.90	C=N stretching
1220-1020	1166.97	1155.40 1078.24	1163.11 1080.17	C-N stretching
1475-1415	1475.59 1417.73		1475.59 1417.73	C-H deformation

Figure 1 FT-IR Studies of Metformin HCl, Guar gum and Physical Mixture



FT – IR Spectra of Guar Gum



FT-IR Spectra of Metformin HCl

Powder X-ray diffraction (PXRD)

X-ray diffraction of Metformin hydrochloride displayed four major peaks marked as 1, 2, 3 and 4 at 2θ : 12.02(23350), 22.42(7900), 25.62(20178) and 38.26 (16146) respectively, while X-ray diffraction of Guar gum resulted in three major peaks at 2θ : 13.69(500), 18.02(590) and 21.65(900) respectively as shown in Table 2. Moreover, X ray diffraction of physical mixture did not result in any significant change either in the intensity of peaks or position of peaks indicating compatibility of Metformin hydrochloride with Guar gum as depicted in Figure 2.

Table 2

PXRD Studies of Metformin HCl, Guar gum and Physical Mixture

Sample	Peak 1 (2θ values)	Peak 2 (2θ values)	Peak 3 (2θ values)	Peak 4 (2θ values)	Peak 5 (2θ values	Peak 6 (2θ values
Metformin HCl	12.02 (23350)	17.80 (2545)	22.42 (7900)	25.62 (20178)	32.42 (2568)	38.26 (16146)
Guar gum	13.69 (500)	18.02 (590)	21.65 (900)			
Physical Mixture	11.26 (22480)	17.69 (2500)	22.54 (8000)	25.26 (20000)	32.36 (2670)	38.42 (16280)

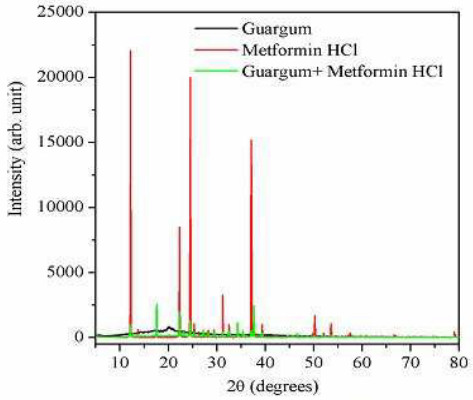


Figure 2. PXRD of of Metformin HCl, Guar gum and Physical Mixture.

Differential Scanning Calorimetry (DSC)

The thermal parameters (T peak), Onset (°C), End set (°C), were obtained from the DSC thermograph for the pure metformin, guar gum, physical mixture. As apparent from the Figure 3, Metformin hydrochloride has a sharp melting endotherm at 254.10 ^{0} C. When metformin was blended with guar gum, a minor shift in Metformin melting endotherm was apparent with changes in the height-to-width ratio of the peaks (Table 3). The reduction in enthalpy of Metformin endotherm is ascribed to the mixing of the components (Figure 3). Thus, no definite solid-solid interaction could be concluded.

Table 3
DSC Studies of Metformin HCl, Guar gum and Physical Mixture

Sample	Onset (ºC)	T Peak(ºC)	End set (ºC)
Metformin HCl	239.92	237.31	254.10
Guar Gum	33.73	82.79	140.54
Physical Mixture	232.68	235.75	248.42

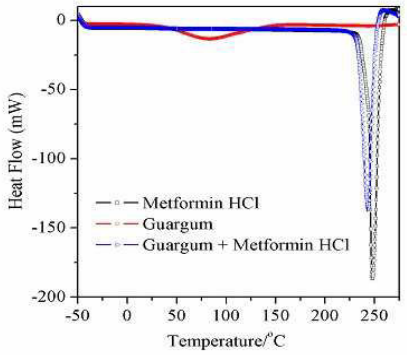


Figure 3 DSC thermogram of of Metformin HCl, Guar gum and Physical Mixture

CONCLUSIONS

From the FTIR spectra, it was concluded that metformin stayed intact, and its rearrangement did not significantly change. Thus metformin-physical mixture was rendered to be compatible. Powder X ray diffraction of metformin-physical mixture did not result in any significant change either in the intensity of the peaks or position of peaks indicating compatibility of the drug. The reduction in enthalpy of metformin's endotherm is ascribed to the mixing of the components. Thus no definite solid-solid interaction could be concluded.

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