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Rudimetary Study of Intrinsic Gemfibrozil with B-Cyclodextrin

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ABSTRACT: The aim of study was carried out the fundamental properties and characterization with the help of equilibrium solubility, phase solubility dissolution rate, drying technique and also use to micro properties by Fourier Transform infrared spectroscopy(FTIR), differential scanningcalorimetric(DSC) and x-ray power diffractometry of poor water soluble,reducing bed cholesterolagent, puretherapeutic compound gemfibrozil[5-(2,5 dimethyle phenoxy)-2,2-dimethylpentonic acid) withcarrier β-cyclodextrin.

Keywords E*quilibrium, drying technique ,Gemfibrozil, Cyclodextrins,*

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I. INTRODUCTION

Complexation process, are based on the ability of many well-known drug to interact and to form new complex drugs with altered properties in comparison with a drug alone. The complication with cyclodextrins (CDs) is an established procedure to improve the biopharmaceutical properties of drugs with poor water solubility [2]. Complexes or coordination compounds, according to the classic definition, result from a donor-acceptor mechanism or Lewis acid-base reaction between two or more different chemical constituents. Complexation is one of several ways to favorably enhance the physicochemical properties of pharmaceutical compounds. It may loosely be defined as the reversible association between two or more molecules to form a nonbonded entity with a well defined stoichiometry. Cycloheptaamylose (cyclodextrins) are useful functional excipients, which are being used in an ever interesting way to camouflage undesirable pharmaceutical characteristics, especially poor aqueous solubility. Chemically they are cyclic oligosaccharides containing at least 6D-(+) glucopyranose units attached by α-(1, 4) glucosidic bonds and available as three natural CDs α-, β- and γ-CDs (with 6, 7 or 8 glucose units respectively) that differ in their ring size and solubility. It has generally been assumed that the mechanism where in, CDs exert their effects, especially their augmentation of solubility, is via the formation of non-covalent, dynamic inclusion complexes [9]^{s}.

II. MATERIALS AND METHODS

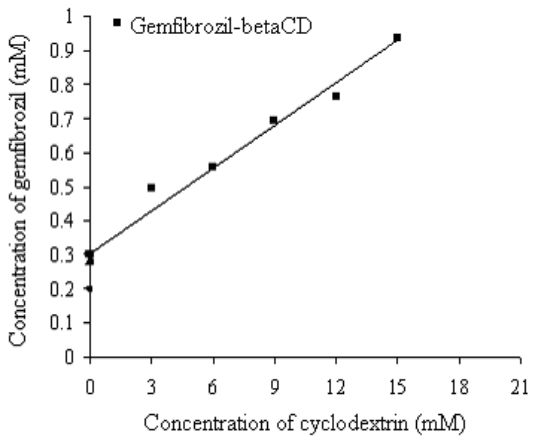
Materials

Gemfibrozil was got as a gift sample from Teva Pharma-ceuticals Limited, India and β-cyclodextrin were as gift sample from Albert David Pvt Ltd, Ghaziabad.

Methods

Equilibrium solubility studies

The soluble complex drugs dried in microwave dried then and add an excess amount of related drugs, to 10 ml of 0.1N Hcl (pH 1.24), double distilled water (pH 6.41) and 0.2M phosphate buffer (pH 7.40). The suspensions were stirred for 3-4 days at 38 °C and filtered through 0.45 µm membrane filter, get diluted and analyzed by UV spectrophotometer at



273nm.

Phase solubility studies

Todetermine the stability constants of for complex gemfibrozil and β-cyclodexrin was to using the phase solubility method [7]. The obtain diagram of Phase solubility with diagrams double distilled waterat 37±0.5 °C. An added to 10 ml aqueous solutions of gemfibrozil containing increasing concentrations of the Cyclodextrin (0-14mmol).

At reaching the equilibrium stage shaken the suspensions at72h .and then they were filtered, appropriately diluted and analyzed by UV spectrophotometer at 274 nm [5, 23]. Toequilibrium theapparent stability constant (Ks) byfollowingequationKs = slope/So (1-slope)…….. (1)

Where, So = Intrinsic solubility of gemfibrozil in the absence of cyclodextrins.

Preparation of mixed complexes

The ratio1:1 molar of both gemfibrozil and CDs complexes were prepared got the results from the preliminary phase solubility suspension.

Used dried complex

A small amount of β-cyclodextrins with water placed in a mortar and mixed to get the homogeneous paste. And add some quantity of gemfibrozil powder in

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homogeneous paste andkneaded 50 min process, some drops of water were added to maintain a suitable consistency. The final mixeredwas dried on a microwave oven at 45 °C for 3 min and the solidwasfinallygroundandsiftedthrougha100meshsieve [6,23].

Evaluation of prepared inclusion

complexes intrinsic dissolution rat studies

To investigate the dissolution behavior by USP apparatus I, rotating disc for optimization of preparation method [20]. A material of disc was made by slow compression of 600 mg of drug mixture in a 14mm IR disc punch and die set (HICON®, India) to compaction pressure of 700Mpa and a dwelling time of 7 min. The compressed disc was seated with wax and successively dipped so that the sides are coated. Compressed pellets of the drug and complexes were dissolution in double distilled water (pH 6.43) that was stirred at 100 rpm and.
Maintained at 37±0.4 °C [2]. At accurate time intervals, 5 ml aliquots were withdrawn and analyzed spectrophotometrically (Shimadzu, pharma spec 1700) at 275 nm. The dissolution was go out in triplicate, and the IDR was determined by dividing the slope of the line by the displayed surfacearea.

Preparation of inclusion complexes

Inclusion complexes (gemfibrozil and CDs) analyzed by various by physiochemical analysis.

Fourier transform infrared (FTIR) spectroscopy

Samples FTIR spectra were obtained by using FTIR spectrophotometer (Perkin Elmer). The prepared and dried complexes. About 2–4 mg of sample was mixed with dried KBr. The samples were scanned from 400 to 2000 cm-1.

Differential scanning calorimetry (DSC)

Differential scanning calorimetry (Perkin Elmer DSC7) measurement The 10 mg samples placed in a suitable pan and fited in a constent disc cell and heat at rate of 15 °C/min over a 60-300 °C temperature range. A nitrogen purge (25 ml/min) was runs through, using an empty sealed pan as a reference. Temperature and heat flow calibrations were performed using indium as a standard.

X-ray diffractometry (XRD)

A Powder sample are used with nikil filtered Cu K patterns were obtained rediation(λ= 1.530498A°) at scan step size of 0.025° under a voltage of 35-50kV and a current of 32mA for the generator. The investigation was performed in the 2θ range of 6-50°.

III. RESULTS AND DISCUSSION

Phase solubility studies-Plotted diram concentration drugs agaistconcentrationthe of CDs at 37°c. Fig-1 Absorbed that solubility of gemfibrozil is increase fixed concenentration range [14].Slop value 0.0611 o fgemfibrozil indicate the molar ratio is 1;1 and [Ks] is 1;1

for β- CDs,respectcompebility calculation as 162.40 $M^{-1.}$ ·overall report is suitable for pharmaceutical utilization[15]. Finally dessolution rate is depend on the relative concentration of drugs.In other hand1;2,1;3 dispersion ratio shows maximum improvement in dessolution rate[1].

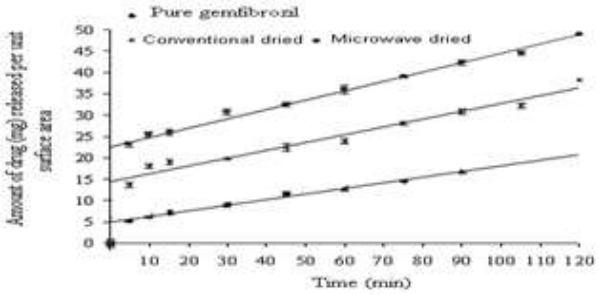

Fig. 2: Intrinsic dissolution profiles of pure gemfibrozil and β- CD
complexes in double distilled water (pH 6.42

Equilibrium solubility studies

The equilibrium solubility of drug and its inclusion complexes in acidic media (0.1N HCl, pH 1.21), double distilled water (pH 6.45) and 0.2M phosphate buffer (pH 7.42) are reported in table 1.Gemfibrozil, the drug showed a very low solubility at pH 1.21 and increased value of solubility's was obtained for dried and microwave dried kneaded complex. It was due to the presence of hydrophilic cyclo dextrin and a better wett ability of the drug.

precipitation	Equilibrium solution(mg/ml)		
	PH	PH	PH
	1.21	6.45	7.42
1.Dried product 2.microwave dried product 3.Gemfibrozil	0.301±0.001 0.532±0.002 0.723±0.002	0.438±0.001. 0.648±0.035 0.082±0.001	1.72±0.02 16.722±0.489 0.302±0.002

Conventionally dried product showed 4.24, 5.72 and 7.98 fold and the microwave dried product showed 7.10, 10.42 and 16.83 fold solubility enhancement at pH 1.23, pH 6.42 and pH 7.40 respectively.

Evaluation of prepared inclusion complexes by intrinsic dissolution ranthe (IDR) studies

Dissolution of gemfibrozil of dried complex, microwave dried complex, are plotted in fig. 2. From IDR plotted diagramfind out dried complexes to be 0.1385 mg $cm^{-1}$and microwave dried 0.1650 mg cm^{-1} min^{-1}respectively and obtain result 1.90 and 2.16 fold greater than .Hence microwave drying superior dying technology to other.

Characterization of prepared inclusion complexes

Fourier transforms infrared spectroscopy

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The infrared spectra of the drug, cyclodextrin, microwave dried and conventional dried complex are presented in fig. 3. Two bands of infrared spectra, at 1705.73 cm^{-1} and at 1043.30 cm^{-1}, 1127.19 cm^{-1} and 1165.76 cm^{-1} (C-O stretching) vibrations are the characteristics infrared spectra of gemfibrozil, used for analysis of the solid state interactions [3]. The spectrum of inclusion complex did not show new peaks which indicates any chemical bonds were created in the prepared complexes [12-22].

In the IR spectra of inclusion complexes, the absorption band at 1043.30 cm^{-1}, 1127.19 cm^{-1} and 1165.76 cm^{-1}

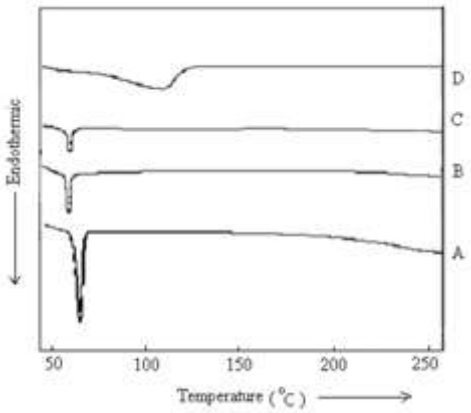


Fig-**3 Fourier transforms infraredspectra of gemfibrozil(a) β-Cyclodexrin (b)dried product (c) microwave product(D)**

disappeared and the intensity of the band at 1705.73 cm^{-1} is also significantly decreased, suggesting hydrogen bonding between gemfibrozil and β-CD in the inclusion complexes.

Differential scanning calorimetry

According to plotted graph of thermogram shown the typical behabour of crysteline solid of gemfibrozil at 65 °C (ΔH=72.236J/g) and CDs ΔH values was 45.176 j/g the ΔH values at dried (45.286J/g) and microwave dried (38.264J/g) where thermal peaks at higher temperatures, strongly grow in intensity of complexation drugs and low to reducess .

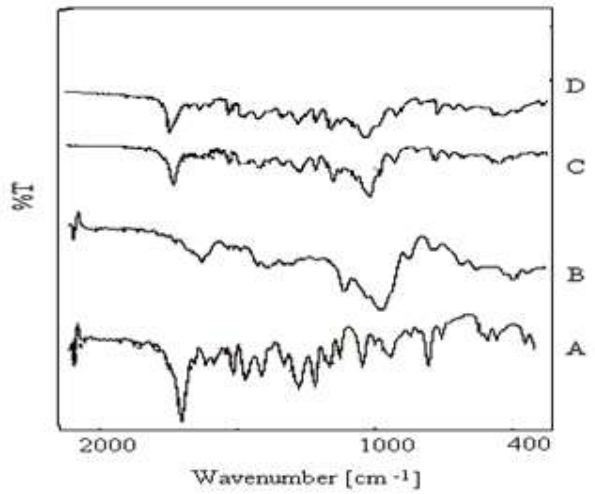
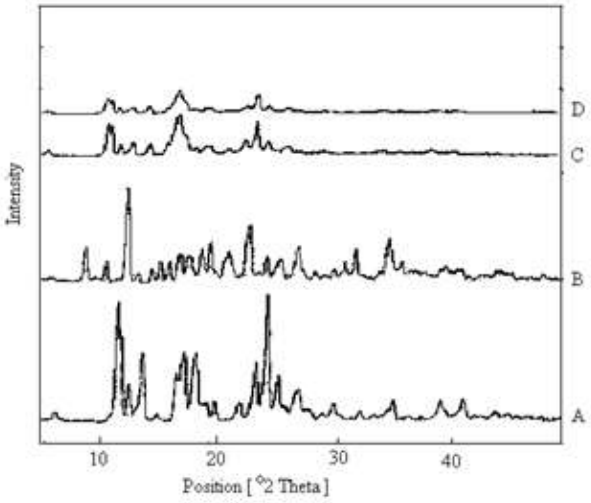


Fig. 4: DSC thermograms of gemfibrozil (A), Conventional dried product (B), Microwave-dried product (C) and β-cyclodextrin (D)

X-ray diffraction analysis (XRD)

The of pure drug and exhibited a crystalline diffraction are represented by XRD patternof pure andβ-CD. in fig. 5.showsl dried and microwave dried product created lesser and broader peaks. Microwave dried product exhibits less distinct diffraction peaks. [12, 21].



IV. CONCLUSION

This study has been eveluted that increase the absorption and solubility rate and other scanig position is better ofpure thearapeticgemfibrozilagaist CDs .with the help of microwave drying technique.s

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