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CHARACTERIZATION OF DIFFERENT CRYSTAL FORMS OF IBUPROFEN, TINIDAZOLE AND LORAZEPAM

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ABSTRACT

Different crystal forms of ibuprofen, tinidazole and lorazepam were prepared and subjected to physicochemical tests like particle size, shape and melting point determination, scanning of U.V., I.R. and N.M.R. Patterns, stability, dissolution and diffusion rate studies. The nature of solvents and method of microprecipitation effect different properties of crystal forms of the drugs.

INTRODUCTION

The degree of crystallinity of drugs can be changed by suitable choice of solvents. Different polymorphs have differences in phylicochemical properties (1 - 4). The present work is undertaken to characterise the different crystal forms of poorly water soluble drugs namely ibuprofen, tinidazole and lorazepam.

MATERIALS AND METHODS

Supercooled and slow cooled variety as well as crystal forms of ibuprofen, tinidazole and lorazepam precipitated from ethanol, chloroform, propyleneglycol and acetone were prepared and labelled

as 1/2/3 control and a,b,c,d,e,f(5). Melting point, average particle size and shape of each physical form were determined.

The U.V. spectra of ibuprofen and tinidazole in 0.1 N NaOH solution and lorazepam in ethanol were scanned using Beckman spectrophotometer model 240. The I.R. spectra of each crystal form of drug in Nujol was scanned in a Perkin Elmer I.R. spectrophotometer. The N.M.R. spectra of each crystal form of ibuprofen and tinidazole were scanned after dissolving them in deuteriated chloroform (CDCL3) and that of lorazepam in deuteriated DMSO using Varian NMR spectrophotometer.

Dissolution study of 100 mg. each of crystal form was conducted using USP XX Dissolution rate testing apparatus in distilled water at 37 degree C and 100 R.P.M. speed. Ibuprofen and Tinidazole sanples were diluted with 0.1 N. NAOH, lorazepam samples were diluted with ethanol and absorbance readings were recorded at 264, 368 and 236 nm respectively using Beckman spectrophotometer(5).

Diffusion study of 10 mg. of each drug sample was conducted by taking 200 ml. of pH 7.4 phosphate buffer as acceptor compartment medium and 30 ml. of pH 8.0 phosphate buffer as donor compartment medium using a 20 mm. dia glass tube with a cellophane membrane as diffusion interphase. The contents of acceptor compartment medium were uniformly stirred at a constant speed and temperature of the medium was maintained at 37 degree C(5).

The stability of each physical form of drug was studied by exposing the samples to 37 degree C. and 85% RH in a high humidity oven.

RESULTS AND DISCUSSION

The nature of solvents and slow cooling or super cooling process may affect the crystal forms, size and shape of drugs. The

TABLE 1
PHYSICOCHEMICAL PROPERTIES OF IBUPROFEN(1) TINIDAZOLE(2) AND LORAZEPAM(3) CRYSTAL FORMS

SAMPLE NO.	METHOD OF PREPARATION	SHAPE AND PARTICLE SIZE (MICRONS)			MELTING POINT (DEGREE C)			PERCENTAGE DRUG DISSOLVED (1/2 HOUR)			DIFFUSION RATE CONSTANT (CM/MIN)			PERCENTAGE DRUG DEGRADATION IN 1 MONTH(85% RH +37 DEGREE C)		
		1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
1,2,3	Received from Market	prismatic (6 - 15)	prismatic (30 - 120)	tubular and Circular (3 - 15)	78	127	170	24.0	88.0	14.3	0.430	0.040	0.040	0	7.7	21
a	Super Cooling	irregular (15 - 40)	irregular (5 - 220)	irregular (15 - 75)	75	125	160	14.3	63.1	17.0	0.315	0.031	0.036	0	25.0	20
b	Slow Cooling	irregular (10 - 30)	irregular (10 - 25)	irregular (10 - 30)	65	115	155	19.3	72.6	21.0	0.243	0.028	0.041	0	23.0	22
c	PPT from Alcohol	circular & needle (3 - 15)	tubular (L30 - 100) (L15 - 20)	tubular (L15 - 95) (W 5 - 10)	73	105	150	33.8	92.2	12.0	0.313	0.033	0.050	5.5	13.5	47
d	PPT from Chloroform	irregular (10 - 20)	prismatic & needle (L40 - 120) (W 6 - 12)	tubular (L15 - 35) (W 2 - 4)	55	112	165	21.9	74.5	14.0	0.150	0.031	0.058	0	9.6	26
e	PPT from Propylene Glycol	circular (2 - 6)	tubular (L20 - 50) (W 3 - 6)	round (2 - 6)	50	85	145	11.9	92.4	18.0	0.451	0.044	0.064	7.0	10.2	37
f	PPT from Acetone	prismatic & Tubular (3 - 10)	tubular (L30 - 100) (L15)	needle (L10 - 15) (W 3 - 6)	80	120	148	4.8	89.2	15.0	0.201	0.035	0.061	0	0	26

TABLE 2

PHYSICOCHEMICAL PROPERTIES OF DIFFERENT CRYSTAL FORMS

Properties	Ibuprofen	Tinidazole	Lorazepam
1. U.V. Spectra (Wavelength Maxima)	175,236,264	176,368	160,236,320
2. Observed changes in I.R.Spectra (CM^{-1})	2800,1580,1400, 800	2800,1800,1400, 1000,800	3000–3600,1600,1400, 1200,800
3. D.S.C. (Melting peaks Control degree K)	352	408.5	470 (Single peak)
a. Supercooled	348	408	–
b. Slowcooled	349	409	–
c. Ethanol ppt	349.5	407.5	418,460 (Two peaks)
d. Chloroform ppt	348	409.5	414,460(Two peaks)
e. Propylene Glycol ppt	350	408	468(Single peak)
f. Acetone ppt	350.5	408	415,456(Two peaks)
4. NMR Spectra (Chemical shift ppm)	1.0,d 1.5, 3H,d 2.4, d 3.8, 1H,q 7.0–7, 4 9H,m 11.5,1H,s		2.5–3. 3,d 4.8d, aliphatic C–H(1) 5.9,d,aliphatic O–H(1) 6.9,d,aliphatic O–H(1) 7.32–7.7,m,aromatic CH(4) 7.6,d of d, aromatic CH(1) 7.3,d, aromatic C–H(1) 11.0, broad singlet,N–H(1) Deuteriation or irradiation of the O–H reduces the methine doublet to a sharp singlet.

crystal forms resulted by precipitation from propylene glycol are having low meting point, circular shape, smaller particle size and higher degradation, dissolution and diffusion rates. Choloroform precipitates have higher melting point, bigger particle size, irregular shape, lower dissolution and diffusion rates and better stability. (Table 1). The U.V. and N.M.R spectra of different crystal forms(Table 2) of each drug namely ibuprofen, tinidazole and lorazepam are identical and superimposable indicating their similarity with respect to their chemical structure and number of hydrogen atoms.

Main differences were observed in I.R.Spectra, X-Ray diffraction pattern and melting peaks of D.S.C. pattern in case of ibuprofen and tinidazole (Table 2). The control sample of lorazepam had single D.S.C. peak whereas the crystal forms resulting after precipitation from ethanol, chloroform and acetone had double D.S.C. peaks (Table 2) indicating the formation of lorazepam solvates with above solvents. Thus polymorphism is predicted in case of ibuprofen and tinidazole due to difference in melting point, X-Ray diffraction pattern and I.R. spectra. Solvate formation of lorazepam is predicted by observing differences in D.S.C. and X-Ray diffraction pattern and in I.R. spectra compared to control sample.

CONCLUSION

Different crystal forms of drugs may be characterised by studying their melting point, particle size, shape, stability and scanning their I.R., X.R.D., N.M.R. and D.S.C. patterns and also by dissolution and diffusion studies. Particles resulting by precipitation from propylene glycol and acetone are having smaller size, circular shape and higher degradation, dissolution and diffusion rates but particles resulting by precipitation from solvents like chloroform have bigger size, irregular shape, lower dissolution and diffusion rates and better stability.

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