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FLUID BED GRANULATION OF IBUPROFEN

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INTRODUCTION:

A number of ibuprofen products have recently been introduced as solid dosage forms. Fluidized bed granulation appears to be an attractive process, considering the physico-chemical properties of ibuprofen.

OBJECTIVE:

To evaluate the effect of selected formulation and process variables using a fluid bed granulation process for ibuprofen granulation and tablet characteristics.

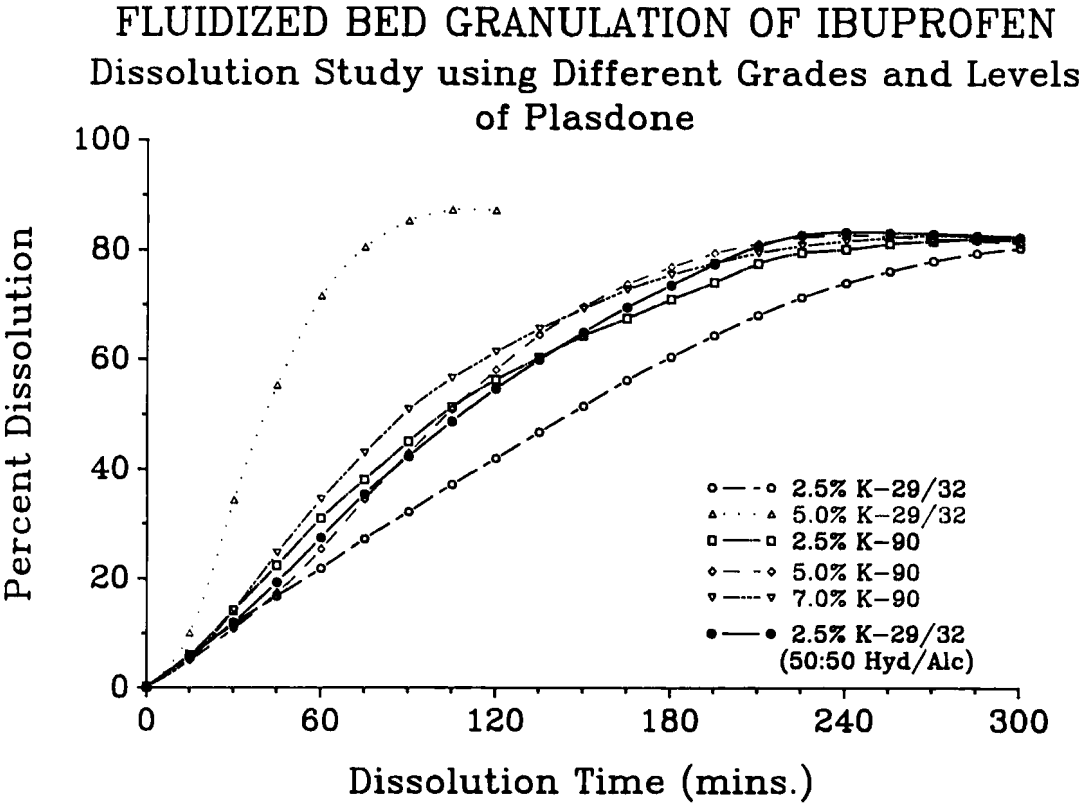
METHODOLOGY:

The study was conducted in three parts:

I) Formulation variables
II) Process variables
III) Effect of disintegrant

Part I: Formulation Variables

Two grades of polyvinyl pyrrolidone, Povidone K-29/32 and Povidone K-90 were evaluated at three levels each (2.5%, 5.0% and 7.5% w/w) as binders using a Glatt fluid bed processor (Model APCG 5/9). The granules formed were evaluated for size, moisture content, density (bulk and tap) and flow rate. The tablets produced from these granules (as is) on a Stokes rotary B-2 tablet press were evaluated for hardness, friability and dissolution characteristics.



FIGURE

Part II: Process Variables

Based on the results of Part I, Povidone K-29/32 was selected as the binder to further evaluate process variables. Various binder addition modes (wet, dry), binder solution concentration (5% w/w, 10% w/w) and drying condition (low 18-40°C, high 39-55°C) were studied. The granules formed and the tablets produced were again evaluated for their properties and characteristics.

Part III: Effect of disintegrant

The information selection was based on the results obtained from Part II. Two percent and five percent w/w Crospovidone were added to selected formulations. The formulations were compressed into tablets and evaluated for their dissolution profile.

TABLE I

EFFECT OF PROCESS VARIABLES

FORMULATION	PROCESS VARIABLES			GRANULE CHARACTERISTICS				TABLET CHARACTERISTICS			
	ADDITION MODE	CONC. OF BINDER SOLN.	DRYING TEMP.	GRANULE SIZE	L.O.D.	DENSITY BULK/TAP	FLOW RATE	HARDNESS	FRIABILITY	DISSOLUTION T-60	DISSOLUTION T-80
		%W/W	°C	% >180μ	%	g/cc	g/sec	KP	%	min.	min.
5% K-29/32	SOLUTION	5.0	LOW	3.0	0.54	0.42/0.48	2.74	13.8	0	123.2	163.4
5% K-29/32	SOLUTION	5.0	HIGH	24.0	0.46	0.43/0.49	6.74	13.8	0	124.1	172.5
5% K-29/32	SOLUTION	10.0	LOW	13.0	0.50	0.34/0.41		14.3	0	103.3	150.0
5% K-29/32	SOLUTION	10.0	HIGH	90.0	0.35	0.32/0.37	3.98	12.1	0	110.0	160.5
5% K-29/32	DRY	5.0	LOW	26.0	0.41	0.45/0.50	1.67	11.0	0	61.5	86.6
5% K-29/32	DRY	5.0	HIGH	57.0	0.40	0.44/0.50	6.34	12.8	0	84.5	116.5

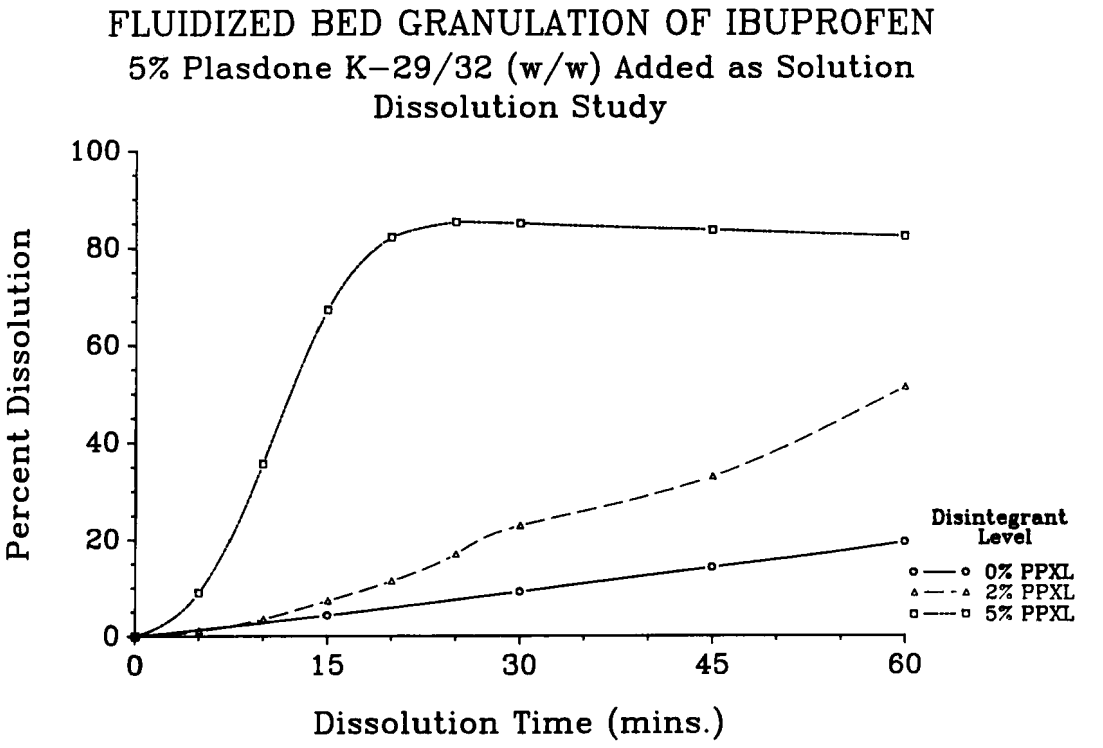


FIGURE 2

RESULTS & DISCUSSION

I. Formulation Variables

Figure 1 illustrates the effect of Povidone type and concentration on the drug dissolution rates. Tablets containing 5% w/w Povidone K-29/32 exhibit significantly faster dissolution rates compared with other formulations. Hence this formulation was selected to further determine effect of certain processing variables.

II. Process Variables

Table I summarizes the effect of process variables, i.e. mode of binder addition (as solution or dry), concentration of binder solution (5 and 10% w/w aqueous solution) and drying temperature (high and low). Based on the data

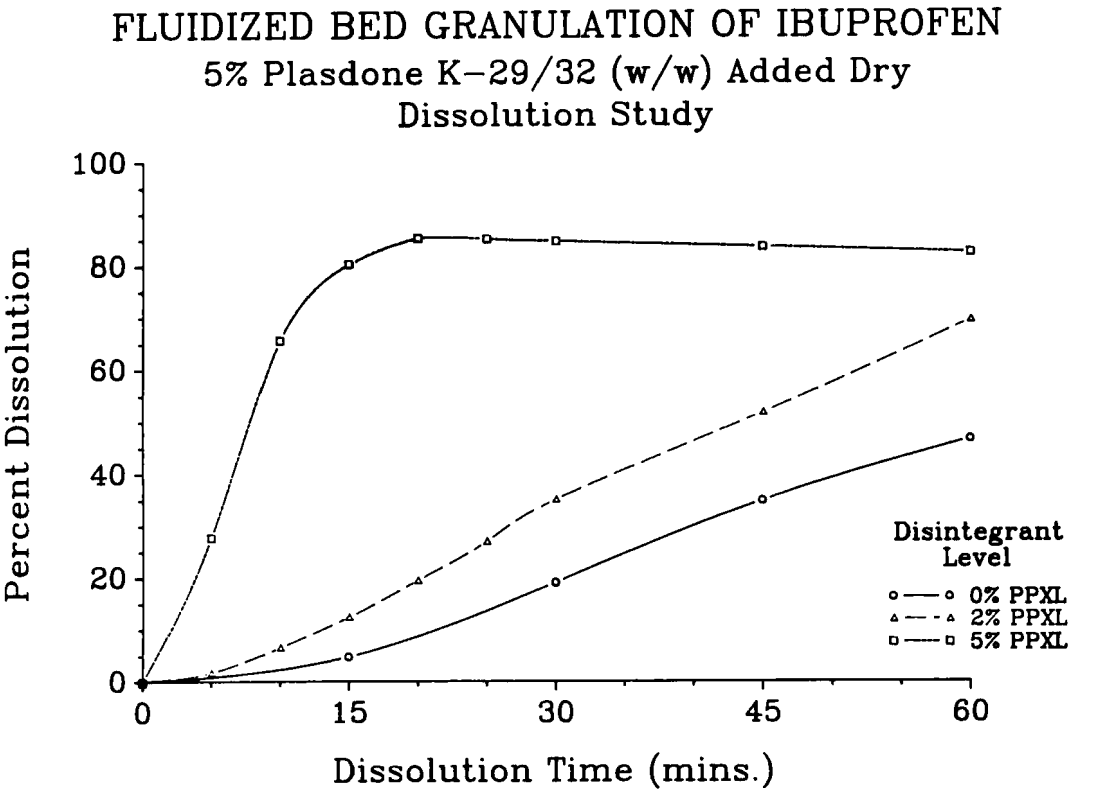


FIGURE 3

presented in Table I, it appears that adding Povidone in the dry form provides a lower T-60 and T-80 when compared with adding Povidone in solution. Similar T-60 and T-80 values were observed when Povidone was introduced as either a 5% or 10% w/w binder solution. However, flow rates obtained with 10% w/w formulation were inadequate. No significant differences were observed in terms of T-60 and T-80 among low and high drying temperatures except when Povidone was added in a dry form.

Granule size, L.O.D., density, hardness and friability values were similar amongst all formulations.

III. Effect of disintegrant

Figures 2 and 3 illustrate rank order correlation in terms of amount of disintegrant added. Higher the amounts of disintegrant, faster the disolution rates.