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EVALUATION AND BIOAVAILABILITY OF PHENAZOPYRIDINE HYDROCHLORIDE TABLETS PREPARED WITH COMPACTROL

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ABSTRACT

Phenazopyridine hydrochloride tablets were prepared at different packing fractions using the newly introduced direct compressible vehicle "compactrol". Tablets were also prepared with avicel and wet granulation technique for comparison.

The physical standards and dissolution rate of the produced tablets were investigated. Also the In-Vivo study for tablets having the highest mechanical strength was carried out. The results revealed that increasing the packing fraction was followed by an increase in tablet hardness and a decrease in friability per cent. Also the disintegration time for tablets prepared by wet granulation technique was increased. However, the dissolution rate of all the produced tablets was slightly affected by the increase in the packing fraction. Compactrol produced the hardest tablets (6 Kg), of the shortest disintegration time (0.17 min.). As regards the bioavailability, avicel produced tablets with the highest bioavailability. On the other hand, the bioavailability of tablets prepared with compactrol and wet granulation was similar. Thus, phenazopyridine tablets can be prepared by direct compression technique to ensure highest mechanical strength and highest bioavailability.

INTRODUCTION

Phenazopyridine hydrochloride is an example of staining drugs[1]. Its tablets were prepared by wet granulation technique. The preparation of these tablets represents a problem for many pharmaceutical manufacturers due to its staining properties to the used machinery and manufacturing rooms.

Direct compression represents the most advanced technique for the formulation of solid dosage forms[2]. The machinery is reduced from several pieces to only a blender and tablet press[3]. Spray-dried lactose, anhydrous lactose, calcium phosphate dextrose, sorbitol and microcrystalline cellulose are examples of the commonly used directly compressible vehicles[3-8]. Recently, compactrol is introduced as direct compressible vehicle due to its high bulk density and free flowing characteristics which impart a high degree of fluidity. This vehicle also requires lower lubricants[9].

The aim of this investigation is to prepare phenazopyridine hydrochloride tablets by direct compression technique to minimize the staining problems encountered during the preparation of its tablets by wet granulation.

Compactrol was used as a direct compressible vehicle for the preparation of phenazopyridine tablets. Avicel as a traditional vehicle and wet granulation techinque were employed to prepare the tablets for comparison. The physical properties and

dissolution characteristics of the tablets were compared at three packing fractions.

In addition, the bioavailability of selected batches from the prepared tablets which exhibit good mechanical properties was also studied.

EXPERIMENTAL

Materials and Equipments:

Phenazopyridine hydrochloride[a], Lactose[b], Avicel-pH 101[c], Compactrol[d], Sucrose[e], Corn starch[c] and Talc[f] were employed.

1. Preparation of Tablets:

1.1- Direct compression:

The tablet matrix consists of 50 parts of phenazopyridine hydrochloride, 100 parts of the vehicle, 15 part of corn starch and 6 parts of talc.

1.2- Wet granulation:

The tablet matrix consists of 50 parts of drug, 100 parts of lactose, 15 parts of corn starch, 6 parts of talc and syrup (30%). The drug, lactose and half of corn starch were mixed and granulated with 30 ml syrup using a sieve No. 8 (B.P.). The obtained granules were dried overnight at 50 C.

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a. Supplied by Elkahira Chem. Co., Cairo. A.R.E.
b. N.V. Hollandsche Melksuiker Fabriek, Uitgeest, Holland.
c. Supplied by El Nile Chem. Co., Cairo, A.R.E.
d. Edward Mendel Co., Carmel, New York.
e. Searl Co., England.
f. El Nasr Chem. Co., Abu Zaabal, A.R.E.

The fraction of granules that passed through sieve No. 20 (B.P.) was collected and mixed with the remaining amount of starch and talc.

1.3- Compression:

Tablets were prepared using a single punch tablet press (Erweka, Type TG 25). Different degrees of compression were obtained by maintaining constant weight while compressing to different thickness, to get different packing fractions[10].

Particle density was calculated by liquid displacement method using benzene[11].

2. Evaluation of Tablets:

2.1- Physical Properties:

Tablets were evaluated for the uniformity of weight (USP), uniformity of thickness (micrometer), hardness (Erweka-Hardness tester), friability (Roche friabilator) and disintegration time (USP).

From the thickness and weight measurements, apparent tablet densities were calculated. The packing fraction of the tablets was obtained by dividing tablet density by the corresponding praticle density[10].

2.2- Dissolution Rate:

The dissolution rate was determined using the USP dissolution apparatus with 500 ml 0.1N HCl in thermostatically controlled water bath at 37 $\pm 1^{\circ}$C and stirring rate of 50 r.p.m. One-ml sample was withdrawn at suitable time intervals and replaced by an equivalent amount of fresh solvent. The samples were suitably diluted with 0.1N HCl and assayed spectrophotometrically for drug content by measuring the absorbance at 430 nm[12].

Evaluation and Bioavailability of Phenazopyridine Hydrochloride Tablets Prepared With Compactrol.

2.3- Bioavailability Study:

Six healthy adult male volunteers 30-35 years age and 60-90 kgm body weight were the subjects chosen. All subjects were refrained from any medications two weeks preceding the experiment. From the prepared tablets, three batchs were selected for bioavailability study, on the basis of their optimal mechanical properties (tablets prepared at high packing fraction). One tablet from the chosen batchs was administered by each subject with about 200 ml of water on an empty stomach. All subjects fasted 1 hr following drug administration. Blank urine was collected before the administration of tablets. Urine was collected quantitatively at time intervals of 1,3,5,7,11 and 24 hours. The collected urine was immediately refrigerated until analysed for the unmetabolized drug spectrophotometrically at 440 nm[13].

RESULTS AND DISCUSSION

1- Uniformity of Weight and Thickness:

Table (1) revealed that, all the prepared tablets except those prepared with avicel exhibit a small coefficient of variation not more than 2%. This may be attributed to the high bulk density and proper flowability of the tablet mixture, consequently complete die filling occurred. On the other hand, tablets prepared with avicel showed a high coefficient of variation exceeding 2%. This may be due to the lower bulk density and bad flowability of the tablet mixture, consequently incomplete

die filling occurred[14]. The uniformity of thickness for the prepared tablets is found to be parallel to those of weight.

It is worhtwhile to mention that, phenazopyridine hydrochloride tablets previously prepared by wet granulation method using calcium carbonate as a diluent were yellow in colour due to fromation of phenzopyridine base[15]. This phenomenon was not met with the formulated tablets specially with compactrol (calcium sulfate dihydrate), where the red colour of phenazopyridine hydrochloride did not change

2- Mechanical Properties:

Table (1) also revealed, that all tablets exhibited good mechanical properties regarding both hardness and friability, except those prepared at a low packing fraction. As the packing fraction was increased, the mechanical properties of tablets increased. The hardest,least friable tablets were prepared with compactrol at the highest packing fraction (6.0 kg at 0.804 packing fraction). These results are in agreement with those recorded by several investigators[10,11,16].

3- Disintegration Time:

As shown from Table (1), all the prepared tablets disintegrated within the USP limits. The disintegration time ranged from 0.17 to 1.42 minutes. Tablets prepared with compactrol showed the least disintegration time (0.17 minute). In addition, it was found that the packing fraction had no significant effect on the disintegration time of tablets prepared with both avicel and compactrol, while a

marked effect was noticed in tablets prepared by wet granulation (0.58 to 1.42 minutes).

4- Dissolution Study:

Figs. (1-3) represent the dissolution profile of the prepared phenazopyridine hydrochloride tablets. It is clear that, the packing fraction has a slight effect on the dissolution profile of the prepared tablets. The percentage of the dissoluted drug at 15 minutes decreased by 10-17% only at high packing fraction. Thus, as the packing fraction increased, the dissolution rate for tablets was slightly decreased. These results are in agreement with literature data[11,17,18].

5- In-Vivo Study:

Fig.(4) shows the mean cumulative percent of unmetabolized phenazopyridine hydrochloride excreted in urine during the 24 hours for the tested formulae. The average excretion rates for the unmetabolized drug from the prepared tablets were calculated. The peak hight and the time of occurrence of the maximum peaks are illustrated in Table 2. It is evident, that the time of occurrence of the maximum peaks was the same for all formulations. This may be due to the high excretion rate of the drug at this period. However, the highest excretion rate was obtained for those tablets prepared with avicel.

In conclusion, Phenazopyridine hydrochloride tablets prepared with compactrol showed the best mechanical properties and the shortest disintegration time. In addition, avicel produced tablets with a highest bioavailability. Thus, it is advantageous to prepare phenazopyridine hydrochloride tablets by direct compression to minimize its staining properties.

Table 1- Effect of Packing Fraction on the Physical Charactristics of Phenazopyridine Hydrochloride Tablets.

Vehicle	Packing fraction	Weight (mg)(x)		Thickness (mm)(x)		Hardness (kg)(x)	Friability (%)(xx)	Disintegration (min)(xxx)
		Average	C.V	Average	C.V			
Avicel	0.716	0.2463	3.33	5.18	3.13	1.75	2.60	0.17
	0.733	0.2451	2.47	5.12	2.91	2.75	0.57	0.33
	0.741	0.2444	3.26	5.07	3.19	3.50	0.49	0.33
Compactrol	0.714	0.2818	1.19	4.87	1.15	1.75	3.66	0.17
	0.758	0.2708	1.04	4.51	1.06	3.00	0.51	0.17
	0.804	0.2725	1.08	4.31	1.06	6.00	0.34	0.17
Wet granulation	0.734	0.2860	0.989	5.20	0.75	2.50	1.48	0.58
	0.750	0.2855	0.880	5.09	0.65	3.75	0.50	0.66
	0.770	0.2848	0.583	4.96	0.43	5.50	0.33	1.42

Average of readings; (x):20, (xx):3 and (xxx):12 .

Table 2-Bioavailability Data for Differently Prepared Phenazopyridine Tablets.

Vehicle	Peak (%)	Peak Time (hours)
Avicel	24.4	2
Compactrol	18.0	2
Wet granulation	12.0	2

Evaluation and Bioavailability of Phenazopyridine Hydrochloride Tablets Prepared With Compactrol.

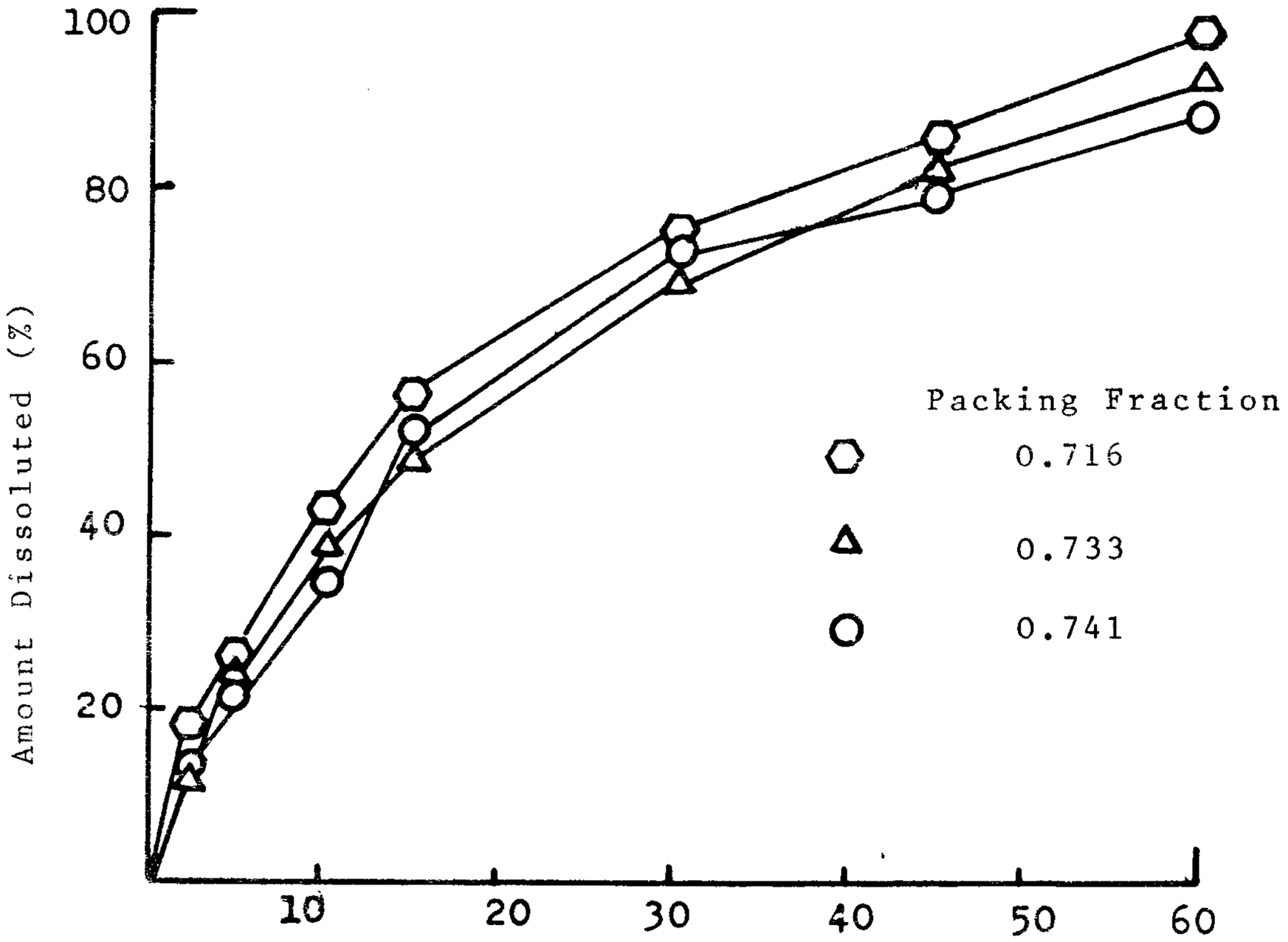

Fig.1--Dissolution Profile of Phenazopyridine HCl Tablets Prepared with Avicel at Different Packing Fractions.

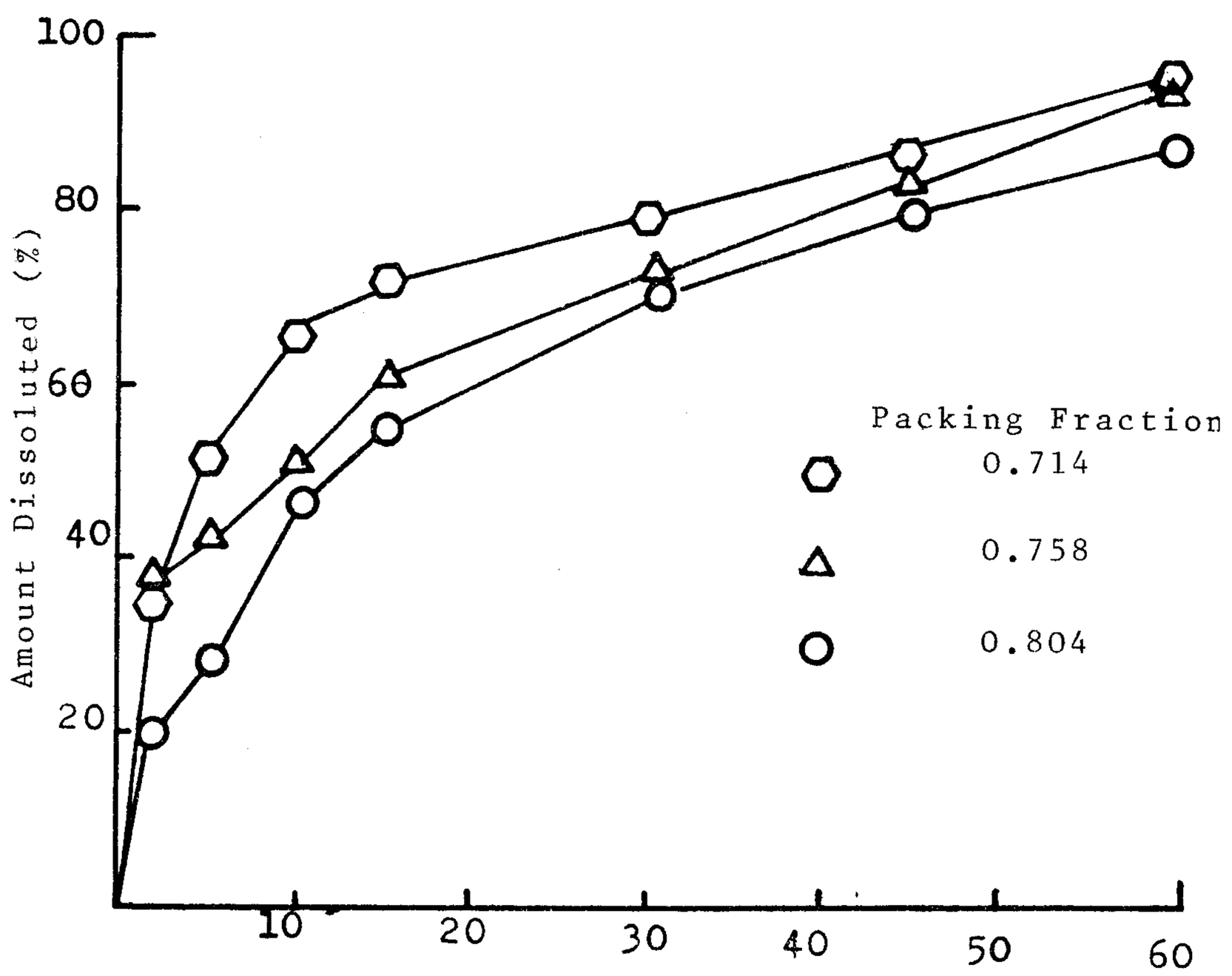

Fig. 2- Dissolution Profile of Phenazopyridine HCl Tablets Prepared with Compactrol, at Different Packing Fractions.

Evaluation and Biloavailability of Phenazopyridine Hydrochloride Tablets Prepared With Compactrol.

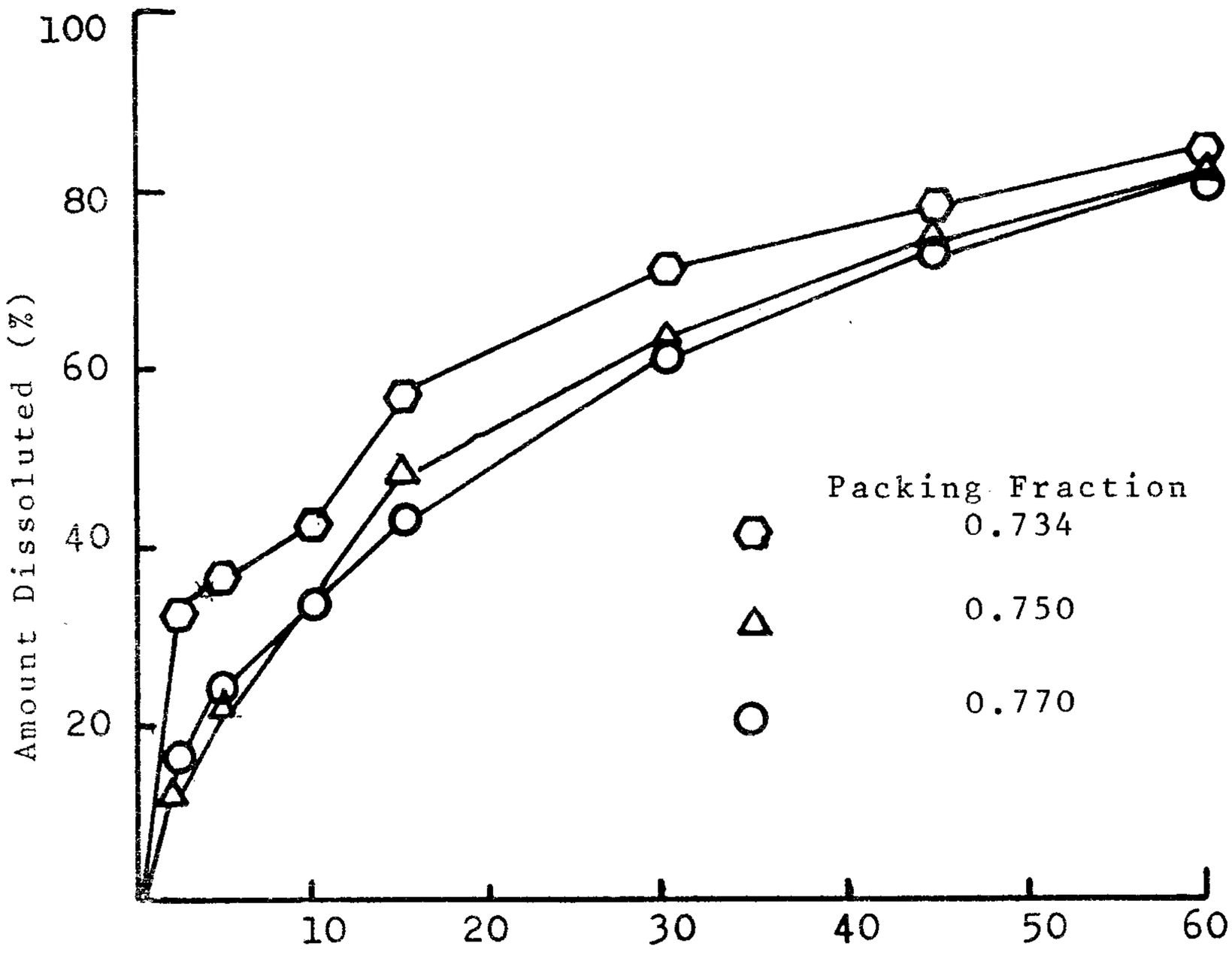

Fig. 3- Dissolution Profile of Phenazopyridine HCl Tablets Prepared by Wet Granulation Technique at Different Packing Fractions.

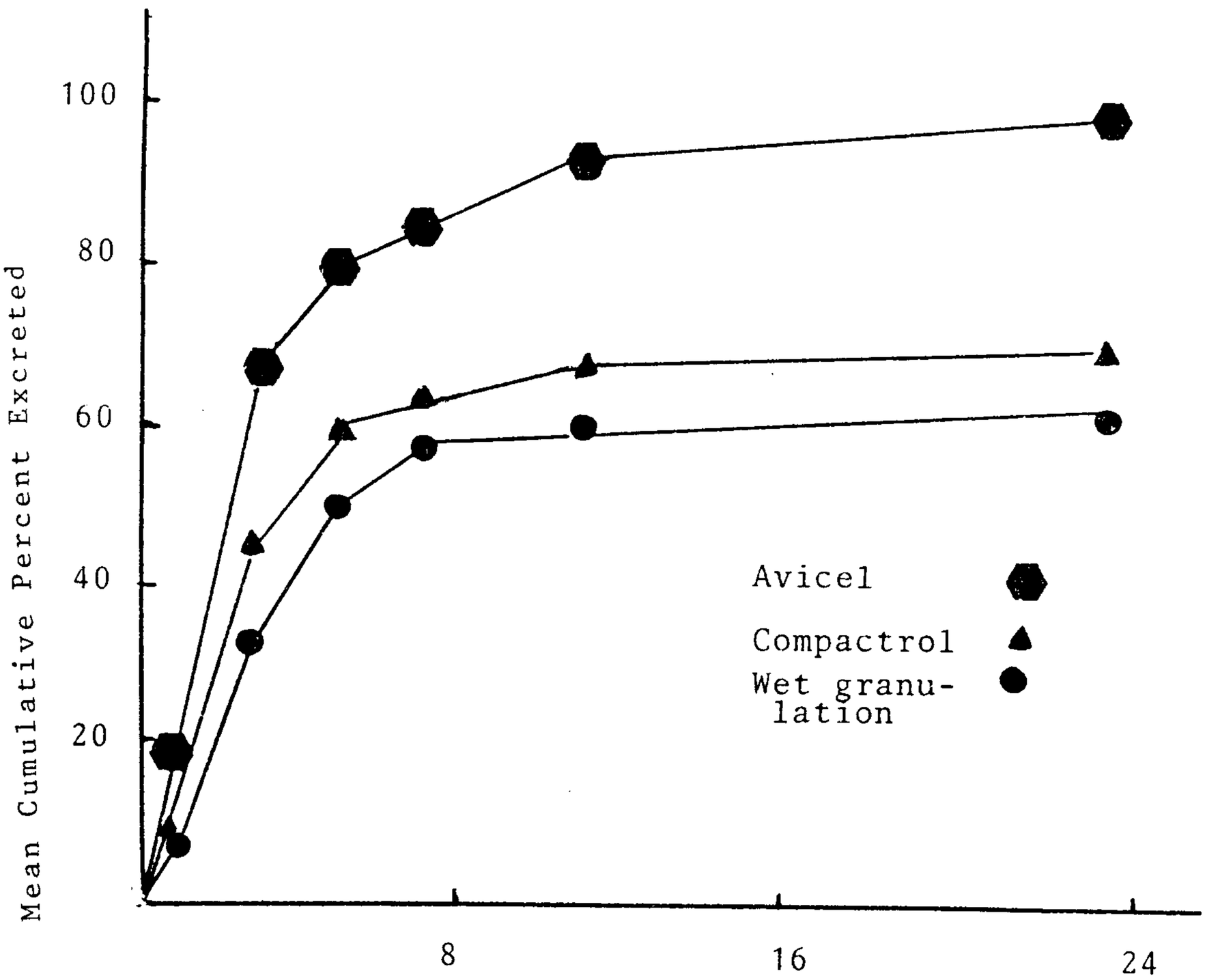

Fig. 4- The Mean Cumulative Urinary Excretion of Phenazopyridine Hydrochloride Tablets.

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تقييم والاتاحة الحيوية لاقراص ايدروكلوريد الفينازوبيريدين المحضرة بالكومبكترول

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تم فى هذا البحث تحضير اقراص ايدروكلوريد الفينازوبيريدين باستخدام طريقة الكبس المباشر عند ثلاث ضغوط مختلفة وذلك باستعمال كل من الكومبكترول والافيسيل كذلك حضرت هذه الاقراص بطريقة التحبيب الرطب تحت نفس الظروف . ولقد قيمت هذه الاقراص من ناحية المقاييس الفيزيقية ومعدل الاذابة ،كما درست الاتاحة الحيوية للاقراص التى تتمتع بخواص ميكانيكية عالية .

ولقد اظهرت الدراسة النتائج الاتية : ـ

١ ـ تزداد صلابة الاقراص وتقل هشوشتها نتيجة لزيادة ضغط الكبس .

٢ ـ يزداد زمن تفتت الاقراص المحضرة بالتحبيب الرطب كلما ازداد ضغط الكبس .

٣ ـ لم يتأثر بشدة معدل اذابة الاقراص بزيادة ضغط الكبس .

٤ ـ كانت اكثر الاقراص صلابة واقل زمن تفتت تلك الاقراص التى حضرت باستخدام الكومبكتول .

٥ ـ اعطى الافيسيل اقراصا تتمتع باعلى اتاحة حيوية .

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