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EVALUATION OF IBUPROFEN-CELLULOSIC POLYMERS SUSTAINED RELEASE TABLETS.

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ABSTRACT

Ibuprofen sustained release tabletse were formulated using wet granulation technique and cellulosic polymers as granulating agents including ethyl cellulose 20, hydroxypropyl methyl cellulose (pharmacoat 606) and hydroxypropyl methyl cellulose phthalate (HP 55 F).

The effect of tablet excipients including Avicel PH 102, Lactose, Emcompress and Emedex on the release rate of ibuprofen from the prepared tablets was also investigated using shift dissolution method.

It was found that among the formulated ibuprofen sustained release tablets, those tablets granulated with 3% w/v ethyl cellulose 20 and containing 23% Emcompress as an excipient were proved to be superior for ibuprofen sustained release. Higher Avicel PH 102 concentration (39 and 40% w/w) was found to enhance the release.

Comparing the effect of 1% w/v of the investigated cellulosic polymers on ibuprofen retardation, it was found to be in the following order : ethyl cellulose 20> HP 55 F> pharmacoat 606.

Various kinetic models including zero order, first order and Higuchi equation were applied to explain the release mechanism from the prepared tablets. It was found that the best fit with the highest correlation coefficient was achieved with the zero-order equation.

INTRODUCTION

The essential requirement in the controlled release system is that the device in some way controls or limits the input of the drug into the body. That is the release from the delivery system rather than the absorption is the critical limiting factor. Such control can be achieved by entrapping the medicament in some insoluble polymers. Cellulosic polymers including ethyl cellulose, pharmacoat 606 and HP 55 F were used for retarding the release of nifedipine[1,2]. Also, metronidazole tablets were prepared by using ethyl cellulose for prolonging the release of the drug which was found to follow zero order kinetics[3]. Ethyl cellulose was also used for retarding the release of theophylline[4,5], chloropheniramine maleate[5] and acetaminophen[5].

Prolonged action pharmaceuticals have received considerable attention within recent years and many physical systems have been designed for providing drugs in a suitable form for maintaining a prolonged action[6-9]. Cooper[10] classified sustained release tablets as follows : (1). Tablets that disintegrate into discrete particles in the GIT, (2) Tablets that gradually eroded but retain their original shape while getting smaller, (po3) Tablets that retain their original shape but give up active drug leaching.

Tablets in the third category may be made by mixing the drug with an inert insoluble, non-absorbable plastic polymers and compressing this mixture into tablets. The present work represents formulating ibuprofen in a sustained release tablets using cellulosic polymers. Wet granulation technique was utilized in formulating such tablets.

The effect of different excipients on drug release was also investigated. Furthermore, the release mechanism of the medicament from the prepared sustained release tablets has been investigated.

EXPERIMENTAL

Materials :

Ibuprofen (Francis S.P., Via Origgio, AV, Italy). Ethyl cellulose 20, hydroxypropyl methyl cellulose 606 and hyroxy propyl methyl cellulose phthlate (Laserson & Sabetay, 14 Rue Jean Ponal, Paris, France). Avicel PH 102, Lactose, Emdex and Emcompress (Edward Mendell Co., New York, USA). Magnesium stearate, dibasic sodium hydrogen phosphate, hydrochloric acid (37%), ethanol (95%) and acetone (Prolabo Co., 12 Rue Pelee, F. 75011, Paris, France). All chemicals were of analytical grade and were used as received.

Equipment :

Dissolution apparatus (Erweka apparatebau, GMbH, Germany).

UV/VIS spectrophotometer (Perkin Elmer Company, Ltd).

Single punch tablet machine fitted with 12 mm concave punches (Frogerais, Type AO, Germany).

Erweka PGS apparatus for making wet granulation, Erweka tablet hardness tester, Erweka tablet friabilator.

Primax mixer (Kl-Kupper, Labor- und Elektronische Gerate, D 5357, Swisttal, Bonn, Germany).

Set of sieves (Mettler, Germany).

Turbula mixer (Willey A. Bachofen Machinen Febrick, Basel, Switzerland).

Methods:

1-Preparation of ibuprofen sustained release tablets:

The specified quantity of the drug powder (0.1 mm mesh screen) was granulated with different concentrations (1,3 and 5% w/v) of alcoholic solutions of cellulosic polymers including ethyl cellulose 20, pharmacoat 606 and HP 55 F. Minimum amount of alcohol was used in the granulation process. The mass was then granulated in the Erweka apparatus through 2 mm mesh screen. The granules were left in a desiccator for 24 hours and then passed through 1 mm mesh screen. The excipients used including Avicel PH 102, lactose, Emcompress and Emdex in the ratios mentioned in Table (1) were added to the granules and mixed for 10 minutes to give a homogeneous incorporation of the drug granules with the filler. Magnesium stearate (1% w/w) was then mixed with the granules for 3 minutes and compressed into tablets. The weights of the tablets for each formula are mentioned in Tablets (4-6). It is worth mentioning that obtaining tablets without the granulating agents was impossible.

2-Evaluation of the prepared tablets:

a-Determination of thickness: The thickness of each tablet was determined by means of a micrometer.
For each batch, 10 tablets were measured.

b-Determination of breaking strength:

It was determined by the Erweka tablet hardness tester. Hardness of 10 tablets of each batch was determined.

c-Determination of friability:

The friability of the produced tablets was determined by calcu

lating the percentage loss in weight of 10 tablets using the Erweka friabilator during 5 minutes at 25 rpm. The experiment was repeated twice and the mean value was considered.

3-Release studies of the prepared tablets :

The dissolution apparatus with a rotating paddle was utilized. One tablet was placed in 1000 ml of the dissolution medium which was previously degassed and warmed to 37°C. The dissolution medium was deionized double distilled water adjusted to pH 1.5 using phosphate buffer. The water bath was maintained at 37°C through the course of the dissolution. At each time interval, 5 ml aliquots were withdrawn from the dissolution medium and were replaced by equal volume of fresh dissolution medium of the same pH. The withdrawn samples were filtered using cotton plug to remove any particulates and assayed for drug content at 222 nm after doing suitable dilutions. This was normalized for the total drug content in the assayed tablet. All assays were done in four replicates to determine the reproducibility of the method and the mean was considered in the calculations.

The pH of the dissolution medium was adjusted initially to pH 1.5 then 100 ml of the dissolution medium was taken every one hour and replaced by the same volume of a solution of pH 7.5, "shift dissolution method"[11]. Thus the measured change of the dissolution medium during the experiment was 1.5, 2.3, 5.9, 6.7, 7.1, 7.2, and 7.3

RESULTS AND DISCUSSION

The composition of the different tablet formulae prepared for iburofen sustained release is shown in tables (1-3). The tablets formulations were 32 formula which contained different types and concentrations of both cellulosic polymers and excipients utilized.

The physical properties of the tested tablet formulations including tablet weight, thickness, hardness, friability, hardness friability ratio (HFR) and drug content are shown in Tables (4-6). As illustrated in the tables, the cellulosic polymers investigated produced tablets of uniform thickness and weight. The formulae 2-8, table (4), containing 23% w/w Avicel PH 102, lactose, Emcompress and Emdex as excipients whow hardness values ranged from 5.5 to 7.8 kg while the formulae 9&10 containing 39 and 49% w/w Avicel pH 102 show higher hardness values (9.2-10.5 kg) and little % loss in friability which was confirmed by the HFR. This observation in formulae 9&10 may be due to the higher concentration of Avicel used as excipient in those formulations[12]. In Table (5), the hardness value reached to 8 kg in formula 20 containing 23% w/w Emcompress and granulated with 10% w/v pharmacoat 606, which may be due to the higher concentration of pharmacoat 606. In Table (6), the hardness values are similar which are not significantly changed from 3.5 to 4.5 kg. concerning friability, big loss was observed for tablets prepared using HP 55 F, which was also confirmed by the HFR, and may be attributed to the binding properties of HP 55 F. These properties may be less than that of ethyl cellulose 20 and pharmacoat 606 respectively.

The release profile of ibuprofen tablets granulated with 1,3 and 5% w/v ethyl cellulose 20 and containing 23% w/w Avicel pH 102 (formula1,2 and 3) are shown in Fig. (1). Increasing the concentration of ethyl cellulose 20 in the tablets matrix leads to delay in ibuprofen release rate, thus 5% w/v ethyl cellulose 20 delayed the T50 of the

drug to 8 hours, Table (7). It is worth mentioning that the shift dissolution method was adopted for investigating the release rate of ibuprofen from the prepared sustained release tablets to simulate the conditions of the pH actually present in the GIT.

The effect of different excipients formulated in the prepared tablets granulated with 3% w/v ethyl cellulose is shown in Fig (2). (formulae 2,4,6, and 7). The dissolution rate of ibuprofen decreased in the following order, Emcompress> Emdex> lactose> Avicel. The highest observed retardation for Emcompress may be due to its slight water solubility. Thus the action of those excipients as ibuprofen retardants may depend mainly on their nature, their water solubilities, and their subsequent effects on the tortuosity factor[13]. The T50% of ibuprofen from those formulae, Table (7), are 345, 465, > 480 and 458 minutes respectively. It is often necessary to add excipients in oral controlled drug delivery systems to either improve the flow properties or alter the drug release rate. Water-insoluble excipients such as Emcompress or water-soluble ones such as lactose may modify the release rates of drugs. Lapidus et al[14], have shown that the addition of lactose increases the release rate of chlorpheniramine than calcium phosphate. Similar findings were obtained[15] on studying the effect of tribasic calcium phosphate and lactose on the release of cibenzoline succinate from plastic matrix tablets. As a water-soluble excipient, lactose dissolved and diffused outward and decreased the tortuosity of the diffusion pathway of the drug. Incorporation of Avicel pH 102 (microcrystalline cellulose), formula 1, caused dramatic increase in ibuprofen release rate which may be attributed to the swelling of microcrystallin cellulose. Further increase in microcrystalline cellulose would burst the tablet, formulae 9&10, resulted in T50% of ibuprofen 196 and 180 minutes, Table (7) and Fig. (3). On the other hand the absence of microcrystalline cellulose, formula 11 caused decrease in ibuprofen release rate (T50% is 480 minutes), Table (7) and Fig. (4).

Increasing the concentration of the excipients, lactose and Emedex in those tablets granulated with 5% w/v ethyl cellulose 20 (formula 5 and 8), resulted in delaying ibuprofen release, Table (7) and Fig. (5) and thus the T50% of ibuprofen from those tablets are 480 and 465 minutes respectively.

Hydroxypropyl methyl cellulose, a hydrophilic matrix was chosen to conduct the retardation of ibuprofen release from tablets. The most used HPMC grade was with nominal viscosity of 4000 mPa.s (measured with a Brookfield viscosimeter on a 2% solution[16]). In the present work, the soluble polymer chosen was the low viscosity HPMC (Pharmacoat 606). The operative principle controlling the drug release from tablet matrix containing such polymers[17] is that on exposure to aqueous fluids the tablet surface becomes wet and the polymer starts to be partially hydrated to form a gelly layer. An initial burst of the drug from the external layer may then happen. There follows an expansion of the gelly layer when water permeates into the tablet increasing the thickness of the gelly layer and soluble drug diffuses through the gel barrier. Concomitantly, the outer layer becomes fully hydrated and dissolves, a process generally referred to as erosion. Water continues to penetrate towards the tablet core until it has been dissolved. The diffusion of the dissolution fluid through the gel is affected by the gel strength. The protective or barrier gel is in turn

controlled by the viscosity and concentration of the polymer used. Examination of the dissolution profiles of ibuprofen tablets granulated with different concentrations of pharmacoat 606 and containing 23% w/w lactose shows that as the polymer concentration increased, the dissolution rate of the drug increased, Fig. (6), (formulae 12,13 lnd 14) and the T50% of ibuprofen decreased, Table (7).

The effect of adding either lactose or Emcompress to ibuprofen granulated with 3% w/v pharmacoat 606 on the drug release rates is shown in Fig. (7), formulae 13 and 17. In this concentration of the granulating agent; Emcompress enhances the dissolution rate of the drug than lactose which could be explained as the concentration of insoluble solid (Emcompress) may affect the sustained release pharmacoat matrices by producing non-uniformity of the gel[18].

The release profiles of ibuprofen in tablets granulated with 5% w/v pharmacoat and containing 23% w/w of different excipients are shown in Fig. (8). The dissolution rate of ibuprofen increased in the order: Avicel> Emcompress> Emedex> lactose. It seems, that granulating ibuprofen with 5% w/v pharmacoat which forms a gelly layer of high strength overcomes the effect of lactose as a tortuosity decreasing factor.

The release profiles of ibuprofen in tablets granulated with 3 and 5% w/w HP 55 F and containing 23% w/w of the different investigated excipients are shown in Figs. (9&10), (formulae 24-30). These profiles demonstrate the influence of the investigated excipients on the release of the drug from the hydrophilic matrices, HP 55 F. Drug release was more rapid from tablets containing Avicel and was the slowest from tablets containing Emcompress. That is because of the swelling effect of the former and the insolubility of the latter. On comparing the effect of the different investigated excipients, the quantities of ibuprofen released after 7 hours were found to be significantly different, Table (7). Thus the T50% of the drug in formulae 24&25 containing 23% w/w Emcompress and granulated with 3 or 5% w/v HP 55 F are > 7 hours, while for formula 30 containing Avicel is 5 hours. These differences may be attributed to the nature of Emcompress at that concentration, 23%, which is considered as a protective to the barrier gel making it formed of the HP 55 F matrix firmer and more cohesive[19] which resulted in slowing the drug release rate.

The release profile of ibuprofen tablets granulated with 1% w/v HP 55 F and containing 23% w/w Emcompress or without excipient is shown in Fig. (11). It is shown that the presence of Emcompress in such a concentration retards the release rate of the drug comparatively. Fig. (12) demonstrates the effect of the granulating agents, ethyl cellulose 20, pharmaccoat 606 and HP 55 F in 1% w/v concentration on the release rates of ibuprofen from tablets formulated without excipients. It is obvious that ethyl cellulose 20 caused maximum retardation of the drug release followed by HP 55 F and pharmacpat 606. Thus it could be stated that it is not only the excipient which controls the drug release but also the nature and the concentration of the polymer used in granulating the drug in the tablet which more significantly controls the drug release rate.

Various equations and various kinetic models were used to investigate the *in vitro* release rates of drugs or from their tablets[20-24]. The release rate constants as well

as their corresponding correlation coefficients (r) of ibuprofen from the prepared tablets were calculated from Higuchi equation (K_H), first order (k_1) and zero order, (K_0), tables (8-10). From the results presented in those tables, it could be concluded that the best fit with the highest correlation coefficients was achieved with the zero-order kinetic equation. The zero-order is : $dQ/dt=K_0$, where Q, is the quantity of the drug released per unit surface area in time t, K_0, is the zero order release rate constant.

The role of dynamic swelling and the dissolution of hydrophilic matrix on the release mechanism were discussed and mathematical models have been developed to allow for the influence of hydration, swelling and glass transition temperature on release rate[25,26]. Korsmeyer et al[27], derived a simple relationship which may be used to describe drug release from polymeric systems in which the release deviates from Fickian diffusion and follows non-Fickian (anomalous) behaviour as follows:

$$\frac{M_t}{M\infty} = Kt^n$$

Where $M_t/M\infty$ is the fractional release of the drug, t is the release time, K is a constant incorporating structural and geometric characteristics of the release device and n is the release exponents indicative of the release mechanism. For instance, n=0.5 for square root of time kinetics and n=1 for zero order release, alternatively :

$$\log \frac{M_t}{M\infty} = \log K + n \log t$$

Table (a) summarizes the general dependence of n on the diffusional mechanism[28].

Table A: Analysis of Diffusional Release Mechanisms.

Diffusional exponent (n)	Overall Solute diffusion mechanism	Time-dependence of solute release rate (dM_t/dt)
0.5	Fickian diffusion	$t^{-0.5}$
0.5<n<1.0	Anomalous(non-fickian) diffusion	t^{n-1}
1.0	case II transport	Zero-order (time-independent release
n>1.0	Super case II transport	t^{n-1}

The n values for the poorly water soluble drug indomethacin with higher concentration of HPMC were 1.07 and 0.90. A value of n=1 would indicate zero-order release from a planar surface[29], but for spheres and cylinders a value of 1 may not correspond to zero-order release due to geometric factors involved in mathematical analysis. The release profile of ketoprofen with HPMC was also zero-order linear[30]. This confirmed the results of ibuprofen with HPMC matrix, Table (9). The higher values of n in some formulae, Table (11), may be due to the influence of : (I). The molecular weight and the molecular size of the polymer, (II) The concentration of the polymer, (III) The dynamic swelling and the dissolution of the polymer matrix and (IV) the effect of adding excipients with hydrophilic polymers on the overall diffusional release of the drug[27-29].

Table 1. The Composition of the Different Formulae Used in the Preparation of the Tablets Containing Ethylcellulose22, as a Granulating Agent

Formula Number	Ibuprofen (%W/W)	Ethylcellulose20* (%W/V)	Excipients+1%Mg.Stearate (W/W)
(1)	76	1	23% AvicelpH102
(2)	76	3	23% AvicelpH102
(3)	76	5	23% AvicelpH102
(4)	76	3	23% Lactose
(5)	60	5	39% Lactose
(6)	76	3	23% Emcompress
(7)	76	3	23% Emdex
(8)	60	5	39% Emdex
(9)	60	5	39% AvicelpH102
(10)	50	5	49% AvicelpH102
(11)	99	1	----------

Ethylcellulose20* was used as the granulating agent.

Table 2. The Composition of the Different Formulae Used in the Preparation of the Tablets containing Hydroxypropyl-Methylcellulose (Pharmacoat 606)

Formula Number	Ibuprofen (%W/W)	Pharmacoat606* (%W/V)	Excipients+1%Mg.Stearate (W/W)
(12)	76	1	23% Lactose
(13)	76	3	23% Lactose
(14)	76	5	23% Lactose
(15)	76	5	23% Emdex
(16)	76	5	23% AvicelpH102
(17)	76	3	23% Emcompress
(18)	76	5	23% Emcompress
(19)	71	5	23% Emcompress+5% HPMC
(20)	66	5	23% Emcompress+10%HPMC
(21)	99	1	----------
(22)	99	5	----------

Pharmacoat606* was used as a granulating agent

Table 3. The Composition of the Different Formulae Used in the Preparation of the Tablets Containing Hydroxypropyl-Methylcellulose Pathalate($HP_{55}f$)

Formula Number	Ibuprofen (%W/W)	$HP_{55}f$* (%W/V)	Excipients+1% Mg.Stearate (W/W)
(23)	76	1	23% Emcompress
(24)	76	3	23% Emcompress
(25)	76	5	23% Emcompress
(26)	76	3	23% Emdex
(27)	76	5	23% Emdex
(28)	76	3	23% Lactose
(29)	76	5	23% Lactose
(30)	76	5	23% AvicelpH102
(31)	99	1	----------
(32)	99	5	----------

$HP_{55}f$* was used as a granulating agent.

Table 4. Effect of Different Concentrations of Ethylcellulose22 and Different Types of Excipients on the Physical Characteristics of Ibuprofen Tablets .

Formula Number	Weight Tablet (mg)	Drug Equivalent (mg)	Thick-ness (mm)	Hard-ness (Kg)	Friability (%Loss)	H.F.R
(1)	405	300	4.50	3.75	0.45	8.33
(2)	405	300	4.47	6.30	0.40	15.75
(3)	405	300	4.50	6.25	0.43	14.50
(4)	403	300	4.48	5.10	0.92	5.50
(5)	420	250	4.65	5.50	0.92	5.98
(6)	406	300	4.45	5.50	0.90	6.22
(7)	404	300	4.55	7.00	0.40	17.50
(8)	420	250	4.60	7.00	0.40	19.50
(9)	500	300	5.30	9.20	0.36	25.46
(10)	500	250	5.30	10.50	0.26	40.38
(11)	405	400	4.55	3.40	1.03	3.30

* The diameter of the prepared tablets was 12 mm.

Table 5. Effect of Different Concentrations of Hydroxypropyl-Methylcellulose and Different Types of Excipients on the Physical Characteristics of Ibuprofen Tablets

Formula Number	Weight Tablet (mg)	Drug Equivalent (mg)	Thick-ness (mm)	Hard-ness (Kg)	Friability (% Loss)	H.F.R.
(12)	405	300	4.55	2.80	0.97	2.89
(13)	406	300	4.55	3.85	0.95	3.21
(14)	407	300	4.56	3.33	1.02	3.27
(15)	402	300	4.50	5.80	0.37	15.68
(16)	405	300	4.55	6.50	0.60	10.83
(17)	400	300	4.45	5.50	1.28	4.30
(18)	405	300	4.55	7.00	1.27	5.51
(19)	425	302	4.60	7.50	1.22	6.69
(20)	460	302	4.70	8.00	1.10	7.27
(21)	405	400	4.60	3.75	0.93	4.03
(22)	405	400	4.65	5.00	0.51	9.80

* The diameter of the prepared tablets was 12 mm.

Table 6. Effect of Different Concentrations of Hydroxypropyl-Methylcellulose Phthalate and Different Types of Excipients on the Physical Characteristics of Ibuprofen Tablets .

Formula Number	Weight Tablet (mg)	Drug Equivalent (mg)	Thick-ness (mm)	Hard-ness (Kg)	Friability (% Loss)	H.F.R.
(23)	405	300	4.50	4.25	1.18	3.60
(24)	406	300	4.50	4.28	1.26	3.18
(25)	406	300	4.50	3.60	1.98	1.82
(26)	404	300	4.48	4.00	1.16	3.45
(27)	400	300	4.46	4.25	0.85	5.00
(28)	405	300	4.55	2.75	1.16	2.37
(29)	402	300	4.55	3.50	1.16	3.02
(30)	400	300	4.50	4.50	1.08	4.17
(31)	405	400	4.60	3.75	1.01	3.71
(32)	405	400	4.65	4.20	0.85	5.06

* The diameter of the prepared tablets was 12 mm.

Table 7. :Time for 50% of Ibuprofen Release from Different Prepared Tablet Formulae.

Formula Number	$T_{50\%}$ (min.)	Formula Number	$T_{50\%}$ (min.)	Formula Number	$T_{50\%}$ (min.)
(1)	218	(12)	405	(23)	>420
(2)	345	(13)	398	(24)	>420
(3)	480	(14)	360	(25)	>420
(4)	465	(15)	338	(26)	330
(5)	460	(16)	338	(27)	368
(6)	>480	(17)	360	(28)	368
(7)	458	(18)	308	(29)	398
(8)	465	(19)	383	(30)	301
(9)	196	(20)	300	(31)	425
(10)	180	(21)	425		
(11)	480	(22)	296		

Table 8. :Mechanism of Ibuprofen Release from Different Prepared Tablets Using Ethylcellulose 20 Matrix.

Formula Number	Zero-Order		First-Order		Higuchi Equation	
	K_0	r_0	K_1	r_1	K_H	r_H
1	47.48	0.974	-0.082	-0.976	138.10	0.927
2	31.45	0.960	-0.067	-0.938	87.49	0.873
3	19.87	0.963	-0.028	-0.948	36.19	0.875
4	12.97	0.959	-0.036	-0.956	55.64	0.882
5	13.92	0.963	-0.030	-0.948	38.79	0.878
6	17.87	0.961	-0.025	-0.955	47.61	0.877
7	21.24	0.943	-0.040	-0.928	58.37	0.848
8	15.82	0.964	-0.035	-0.951	44.11	0.879
9	50.97	0.979	-0.208	-0.936	149.14	0.937
10	37.66	0.970	-0.190	-0.941	112.50	0.905
11	22.42	0.945	-0.030	-0.935	61.81	0.856

K and r are the release rate constant and correlation coefficient respectively.

Table 9 :Mechanism of Ibuprofen Release from Different Prepared Tablets Using Hydroxypropyl-Methylcellulose Matrix.

Formula Number	Zero-Order		First-Order		Higuchi Equation	
	K_o	r_o	K_1	r_1	K_H	r_H
12	23.90	0.925	-0.044	-0.962	64.93	0.822
13	24.55	0.932	-0.045	-0.905	66.91	0.831
14	26.92	0.955	-0.056	-0.919	75.08	0.872
15	24.31	0.966	-0.044	-0.951	68.25	0.887
16	43.41	0.978	-0.146	-0.971	126.95	0.936
17	31.51	0.918	-0.077	-0.850	85.42	0.814
18	31.66	0.968	-0.079	-0.914	88.35	0.876
19	25.69	0.965	-0.057	-0.930	71.67	0.898
20	32.44	0.978	-0.077	-0.957	92.15	0.909
21	28.41	0.926	-0.040	-0.905	77.24	0.824
22	51.66	0.965	-0.096	-0.939	144.72	0.884

Table 10 :Mechanism of Ibuprofen Release from Different prepared Tablets Using Hydroxypropyl-Methylcellulose Phthalate Matrix.

Formula Number	Zero-Order		First-Order		Higuchi Equation	
	K_o	r_o	K_1	r_1	K_H	r_H
23	15.82	0.942	-0.026	-0.932	43.37	0.845
24	20.71	0.938	-0.036	-0.912	56.50	0.838
25	22.58	0.929	-0.041	-0.906	61.48	0.827
26	34.51	0.951	-0.080	-0.912	95.20	0.858
27	27.99	0.932	-0.056	-0.908	76.56	0.834
28	28.82	0.941	-0.059	-0.904	79.14	0.846
29	25.27	0.943	-0.048	-0.928	69.37	0.847
30	37.68	0.963	-0.089	-0.940	105.57	0.883
31	28.79	0.941	-0.048	-0.927	79.84	0.845

K and r are the release rate constant and correlation coefficient respectively.

Table 11 :The Effect of Ibuprofen With Hydroxypropyl-Methyl cellulose Matrix on the Exponent (n) Derived from Dissolution Data

Formula Number	(n)	Formula Number	(n)
(12)	2.4	(17)	2.2
(13)	2.2	(18)	1.3
(14)	1.3	(19)	2.1
(15)	1.4	(20)	1.5
(16)	1.4	(21)	2.2

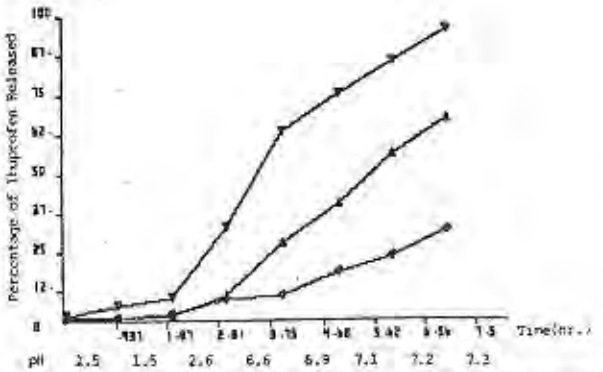

Fig. 1 :Release Profile of Ibuprofen Tablets 300mg Granulated With Different Concentrations of Ethylcellulose20 and 23% Avicel, Using Wet Granulation Technique and Shift Dissolution Method.
Key : ▼ Ibuprofen Tablets With 1% Ethylcellulose20, ▲ With 3% Ethylcellulose20, ● With 5% Ethylcellulose20.

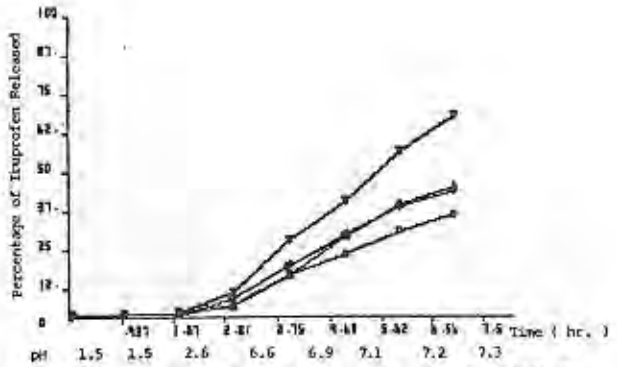

Fig. 2 :Release Profile of Ibuprofen Tablets 300mg, Granulated With 3% Ethylcellulose20 and Mixing After that With 23% of Different Filler,Using Wet Granulation and Shift Dissolution Method.
Key : ▼ Ibuprofen Tablets With 23% Avicel, ● With 23% Lactose, ▲ Ibuprofen Tablets With 23% Emdex , ■ With 23% Encompress.

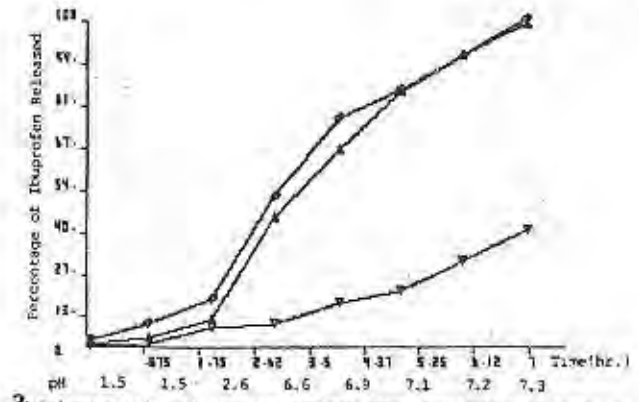

Fig. 3 :Release Profile of Ibuprofen Tablets 300mg Granulated With 5% Ethyl-cellulose20 and Different Concentrations of AvicelPH102,Using Wet Granulation Technique and Shift Dissolution Method
Key : ▼ Ibuprofen Tablets With 23% Avicel, ▲ With Avicel, ● With Avicel.

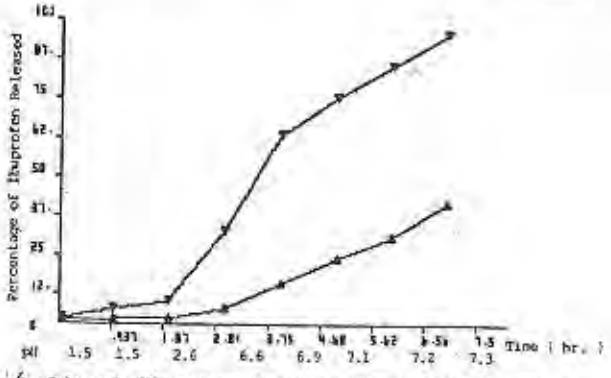

Fig. 4 :Release Profile of Ibuprofen Tablets 300mg (With 23% Avicel) and 400mg (Without Avicel) ,Both Granulated With 1% Ethylcellulose20 Using Wet Granulation Technique and Shift Dissolution Method.
Key : ▼ Ibuprofen Tablets (With 23% Avicel), ▲ Ibuprofen Tablets (Without Avicel).

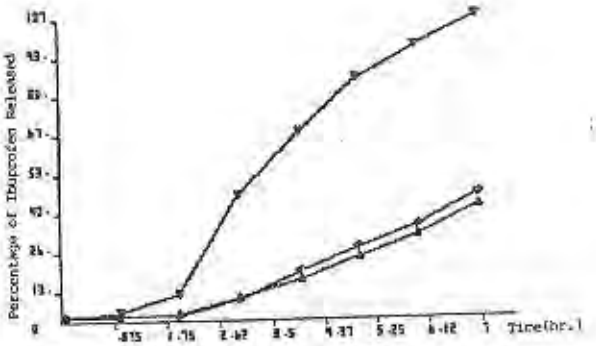

Fig. 5 :Release Profile of Ibuprofen Tablets 300mg, Granulated With 5% Ethylcellulose20 and Mixing After that With 40% of Different Filler Using WET Granulation and Shift Dissolution Methods.

Key : ▼ Ibuprofen Tablets With 40% Avicel, ▲ With 40% Lactose, ◆ With 40% Endex.

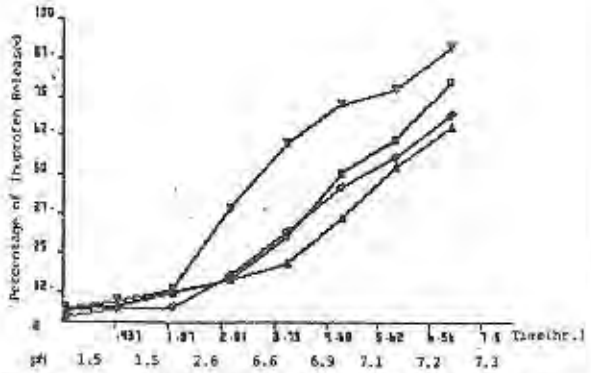

Fig. 8 :Release Profile of Ibuprofen Tablets 300mg,Granulated With 5% Pharmacoat606 and 23% of Different Excipients,Using Wet Granulation Technique and Shift Dissolution Method

Key : ▼ With 23% Avicel, ▲ With 23% Lactose, ◆ With 23% Endex, ■ With 23% Encompress.

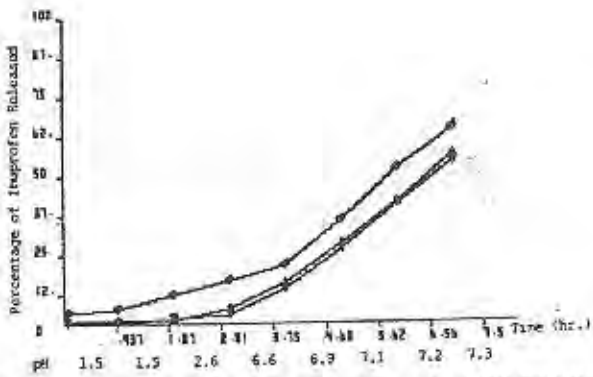

Fig. 6 :Release Profile of Ibuprofen Tablets 300mg, Granulated With Different Concentrations of Pharmacoat606 and 23% Lactose, Using Wet Granulation Technique and Shift Dissolution Method.

Key : ▼ Ibuprofen Tablets With 1% Pharmacoat, ▲ With 3% Pharmacoat, ◆ With 5% Pharmacoat.

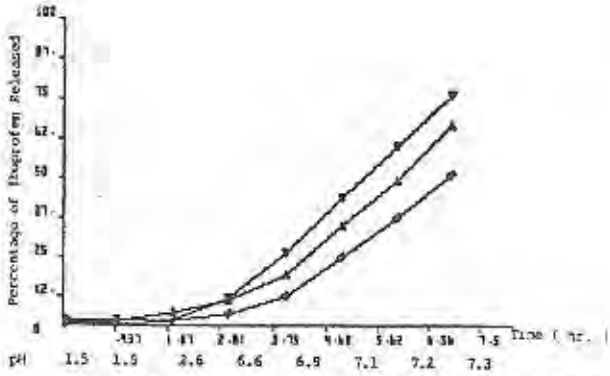

Fig. 9 :Release Profile of Ibuprofen Tablets 300mg Granulated With 3%$HP_{55}F$ and Mixed After that With 23% of Different Excipients,Using Wet Granulation Technique and Shift Dissolution Method.

Key : ▲ Ibuprofen Tablets With 23% Lactose, ▼ With 23% Endex, ◆ With 23% Encompress.

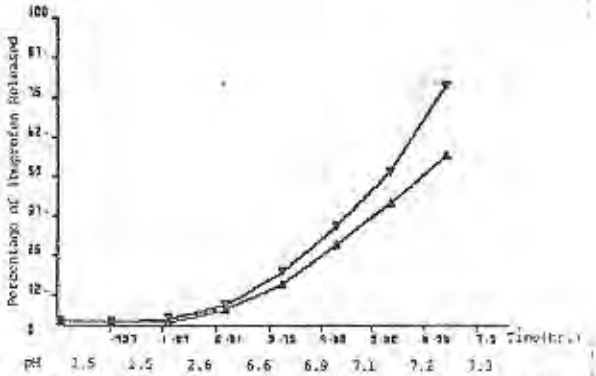

Fig 7 :Release Profile of Ibuprofen Tablets 300mg,Granulated With 3% Pharmacoat606 and Mixing After that With 23% of Different Excipients,Using Wet Granulation and Shift Dissolution Method.

Key : ▼ Ibuprofen Tablets With 23% Encompress, ▲ With 23% Lactose.

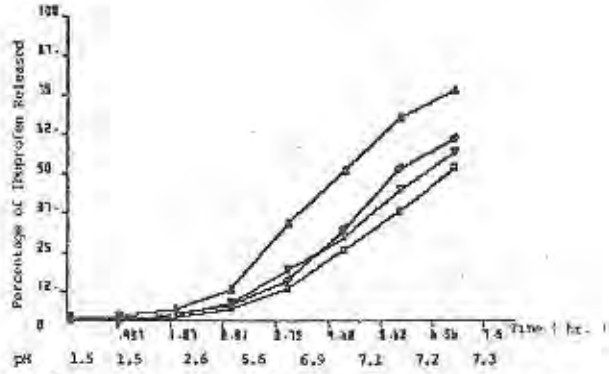

Fig. 10 :Release Profile of Ibuprofen Tablets 300mg,Granulated With 5% $HP_{55}F$ and Mixed After that With 23% of Different Excipients Using Wet Granulation Technique and Shift Dissolution Method.

Key : ▲ Ibuprofen Tablets With 23% Avicel, ▼ With 23% Lactose, ◆ Ibuprofen Tablets With 23% Endex , ■ With 23% Encompress.

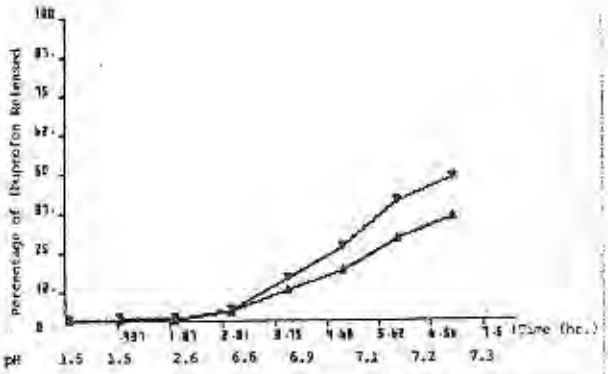

Fig. 11 :Release Profile of Ibuprofen Tablets 400mg (Without Excipients), and Ibuprofen Tablets 300mg (With 23% Encompress), both Granulated With 1% $HP_{55}P$ Using Wet Granulation and Shift Dissolution Method.

Key : ▼ Ibuprofen Tablets (Without Excipients).
▲ Ibuprofen Tablets (With 23%Encompress).

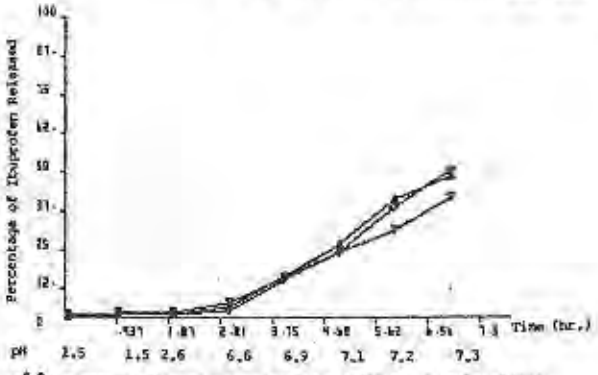

Fig. 12 :Release Profile of Ibuprofen Tablets 400 mg, Granulated With 1% Ethylcellulose 20, 1% $HP_{55}P$,and 1% Pharmacoat 606 (Without Excipients) Using Wet Granulation Technique and Shift Dissolution Method.

Key : ▼ 1%Ethylcellulose, ▲ 1%$HP_{55}P$, ◀ 1%Pharmacoat606.

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تحضير وتقييم أقراص ممتدة المفعول لعقار أبيوبروفين مع البوليمرات السليلوزية

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حضرت أقراص أبيوبروفين ممتدة المفعول باستعمال التحبب المبلل والبوليمرات السليلوزية كعامل محبب وشملت ايثيل سليلوز ٢٠ ، هيدروكسى بروبيل ميثيل سليلوز ، هيدروكسى بروبيل ميثيل سليلوز فيثالات.

ولقد درس تأثير بعض صواغات الأقراص على اتاحة العقار من أقراصه المحضرة ولقد شملت هذه الصواغات الأفسيل واللاكتوز والامكمبرس والامدكس وذلك باستخدام طريقة تغيير الاسى الهيدروجينى فى وسط الاتاحة.

ولقد حققت الأقراص المحضرة باستخدام ٣٪ وزنا/حجم ايثيل سليلوز كعامل محبب وتحتوى على ٢٣٪ وزنا/وزن امكمبرس على اطول اتاحة للعقار موضوع الدراسة - بينما اسرع الأفسيل فى تركيزات عالية (٣٩٪ ، ٤٩٪ وزنا/وزن) من سرعة اتاحة العقار من الأقراص موضوع الدراسة.

وفى تركيز ١٪ وزنا/حجم من البوليمرات السليلوزية كعوامل محببة وجد أن الايثيل سليلوز ٢٠ قد حقق اطول اتاحة للعقار من الأقراص المحضرة.

ولقد درست ميكانيكية اتاحة ابيوبروفين من الأقراص المحضرة بواسطة معادلة من رتبة الصفر ، معادلة الرتبة الاولى ، معادلة هجوشى.

وقد وجد ان أفضل تمثيل لذلك هو المعادلة رتبة الصفر.

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