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STUDIES ON DISSOLUTION RATE OF PARACETAMOL TABLETS BY USING DIFFERENT POLYMERS

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ABSTRACT

Paracetamol is an analgesic and anti-pyretic drug which is poorly soluble in water. Trend towards formulations of dispersible tablets is evident throughout the world. The main of this study is to formulate Paracetamol fast dissolving tablets and to study the effect of various hydrophilic polymers and disintegrating agents on drug releasing characteristics of the prepared Paracetamol dispersible tablets. Magnesium sterate, Talc, Polyvinyl pyrolidine (PVP), potato starch, Hydroxy propyl methyl cellulose (HPMC-4000), Primogel are used as excipients. Paracetamol dispersible tablets are prepared by wet granulation method. The prepared formulations were passed the evaluation test that is weight variations, Percentage drug content, and disintegration, Uniformity of dispersion, Hardness & friability. When compared to potato starch, the Primogel is showing better increase in rate of dissolution of prepared tablets. Out of those three formulations F2, F3 and F4 in which Primogel (5%) used as extra disintegrating agents was used.F4 was showing better increase in rate of dissolution of drug.F4 was prepared by solid dispersion of Paracetamol with PVP. First order rate constant values: K2<K3<K4 Regression Coefficient values: R2<R3<R4.

KEY WORDS: Paracetamol, Primogel, Potato starch, Talc, HPMC, PVP, Dissolution rate.

INTRODUCTION:

The oral route of administration is the most important method of administering drugs for systemic effects .Nevertheless ,it is probable that at least 90% of all drugs used to produce systemic effects are administered by the oral route .Tablets are intended for oral administration, some are swallowed whole, some after being chewed. Some are dissolved or dispersed in water before being administered and some are retained on the mouth, where the active ingredients are liberated .tablets are mainly used for systemic effect drug delivery. For systemic use drug must be released from tablets that dissolved in fluids of the mouth, stomach and intestine and then absorbed in to systemic circulation by which it shows its therapeutics effects[6].

Tablets and capsules represent unit dosage form in which one usual dose of the drug has been accurately placed[1]. By comparison, liquid dosage form are usually designed to contain one dose of medication in 5-30ml.the patient is then asked to measure his or her own medication using teaspoon ,tablespoon or other measuring devices. Such dosage measurements are typically error by a factor ranging from 20-50% when the drug itself the patient. Liquid dosage forms have also other disadvantages when compared to the tablets[2].

Paracetamol is an analgesic and anti pyretic drug which is poorly soluble in water. Formulation of Paracetamol as rapid dissolving tablets are advantageous over the conventional as they disintegrates easily and enhancing fast dissolving their by fast absorption and fast onset of action, resulting in faster exhibition of therapeutic responses .hence, these Paracetamol rapid dissolving tablets are preferable than conventional .this also help to improve patient compliance.

The trend towards formulations of dispersible tablets is evident throughout the world. for example, it is understood that all the tablets marked in nevertheless must have the ability to form adequate dispersion when placed in water.[5]They have stability characteristics of other solid dosage forms. The dispersible tablets are uncoated tablets that produce a uniform dispersion in water[3].

The main of this study is to formulate Paracetamol fast dissolving tablets[4] and to study the effect of various hydrophilic polymers and disintegrating agents on drug releasing characteristics of the prepared Paracetamol dispersible tablets.

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APPARATUS AND EQUIPMENTS:

Monsanto hardness tester, disintegration test machine IP/BP/USP standards (Campbell electronics, Bombay), Digital electronic balance (Campbell electronics, Bombay) cadmach semi automatic single punch tablets press (cadmach type no: CMS -25, Serial No: H/464/98, Ahamadabad)Digital Rou Digital electronic balance (Campbell electronics, Bombay) cadmach semi automatic single punch tablets press (cadmach type no: CMS -25, Serial No: H/464/98, Ahmadabad) Digital Roches friabilator(Campbell electronics, Bombay)

CHEMICALS:

Paracetamol, Magnesium Sterate, Talc-Yarrow–Chem. Products, Dombivli), Polyvinyl pyrolidine (PVP), potato starch, Hydroxy propyl methyl cellulose (HPMC-4000), Primogel from S.D Fine chem. LTD.

METHOD OF PREPARATION:

WET GRANULATION METHOD:

By using potato starch as disintegrating agent

The Required quantity of Paracetamol, Polyvinyl pyrolidine (PVP-2%) and potato starch-5% as inter granular disintegrating agent were mixed thoroughly in a mortar and ethyl alcohol was added drop wise to get the damp mass. this damp mass was passed through a sieve no:16. The obtained granules were dried in hot air oven at 60ºC.The obtained dried granules were again passed through sieve no: 120. Now potato starch (5%) as extra granular disintegrating agent. the bolted Magnesium sterate, Talc-(2%) were added one by one to obtained granules and mixed uniformly.

By using Primogel as Super-disintegrating agent:

The Required quantity of Paracetamol[9], Polyvinyl pyrolidine (PVP-2%) were mixed thoroughly in a mortar and The obtained ethyl alcohol was added drop wise to get the damp mass. this damp mass was passed through a sieve no:16.granules were dried in hot air oven at 60ºC.The obtained dried granules were again passed through sieve no: 16. Now Magnesium sterate passed through sieve no: 120. Now Primogel (5%), the bolted Magnesium sterate, Talc-(2%) were added one by one to obtained granules and mixed uniformly.

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By using two different polymers (HPMC,PVP) and Primogel as Super-disintegrating agent:

The Required quantity of Paracetamol, Polyvinyl pyrolidine (PVP-10%), HPMC-4000(10%) were weighed. in two different beakers. Sufficient quantity of ethyl alcohol was taken. Required quantity of Paracetamol was dissolved in to beaker containing ethyl alcohol. Dissolve PVP in one beaker containing paracetamol solution and HPMC in another beaker. There were mixed thoroughly and kept in hot air oven at 90ºC. For evaporation of ethyl alcohol solvent. The resultant drug-polymer mixtures were taken separately in mortars.PVP-2%was added to each of the above mixtures and mixed uniformly. To this ethyl alcohol was added drop wise to get the damp mass. This damp mass was passed through a sieve no: 16. The obtained granules were dried in hot air oven at 60ºC.The obtained dried granules were again passed through sieve no: 16. Now Magnesium sterate passed through sieve no: 120. Now Primogel (5%), the bolted Magnesium sterate (2%), Talc-(2%) were added one by one to obtained granules and mixed uniformly[7].

FORMULATION OF TABLETS:

The granules of F1, F2, F3, and F4 were compressed with 9mm punches by Cadmach semi automatic single punch press the hardness of the tablets was adjusted to optimum levels with required amount of compression force. The resultant tablets were stored in container.

EVALUATION OF TABLETS:

The formulated tablets were evaluated for the following physicochemical characteristics.

General appearance: The formulated tablets were assessed for its general appearance.

Weight variation: Formulated matrix tablets were tested for weight uniformity.20 tablets were weighed collectively and individually .from the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to ascertain whether it is within permissible limits or not.

Hardness: Hardness of tablets was determined by using Monsanto hardness tester. The lower plunger was placed in contact with the tablets and a zero reading was taken. The plunger was then forced against a spring by tuning a threaded bolt until the tablet fractured .as the spring was

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compressed a pointer rides along a gauge in the barrel to indicate the force[8].

Friability: The Roche friability test apparatus was used to determine the friability of the tablets 20 pre-weight tablets were placed in the apparatus, which was given 100 revaluations. After which the tablets were reweighed. The percentage friability was calculated.

ASSAY OF PARACETAMOL:

Weigh and powdered 20 tablets .weighed accurately a quantity of powder equivalent to 0.15gms of paracetamol and 50ml of 0.1M NaoH, diluted with 100ml of water, shacked for 15 minutes and add sufficient water to produce 200ml.mixed and filtered and diluted 10ml of filtrate to 100ml with water. To 10ml of resulting solution add 10ml of 0.1 M NaoH dilute to 100ml with water and measure the absorbance of the resulting solution at about 256nm.

DISSOLUTION TEST: Dissolution test were carried out to determine the amount of drug released during a specific period of time using I.P apparatus-I.

REQUIREMENTS:

Phosphate buffer PH-7.8, Digital dissolution rate test apparatus of Campbell electronics.

PREPARATION OF PHASPHATE BUFFER PH-7.8: Place 50ml of 0.2M potassium dihydrogen phosphate in 200ml volumetric flask, add 44.5ml of 0.2M NaoH and then add water to final volume.

POTASSIUM DIHYDROGEN PHOSPHATE (O.2M): Dissolved 27.218 gms of potassium dihydrogen phosphate in water and dilute with water to 1000ml.

PROCEDURE:

At first 900ml of dissolution medium was placed in bath container. The tablet was introduced in to the bath container, the paddle was rotated at 50RPM up to 1 hr .5ml of sample solution was withdrawn from batch container and again 5ml of fresh dissolution medium was replaced into the bath container to maintain the constant volume.

Thus the sample withdrawn within the specified time intervals such as 5,10,15,20,25,30,35,40,45,50,55 and 60 minutes. The obtained sample solution were subjected to 1 in 10 dilutions by using phosphate buffer PH-7.8.The obtained sample solutions optical densities were measured at maximum at about249nm against the blank using spectrophotometer. The absorbance values were noted.

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TABLE: 1: The percentage drug release from the formulation:

Time (Min)	F1	F2	F3	F4
O	0	0	0	0
5	18.1	10.1	12.6	13.5
10	23.3	13.6	23.7	14.5
15	35.1	22.1	32.4	23.3
20	40.7	28.1	45.3	35.5
25	47.4	37.6	55.2	43.4
30	53.5	52.6	62.6	56.5
35	54.8	54.4	68.4	77.1
40	57.3	56.6	76.8	78.1
45	62.5	60.3	80.4	84.5
50	64.9	70.9	81.5	85.1

GRAPH: 1The percentage drug release from the formulation:

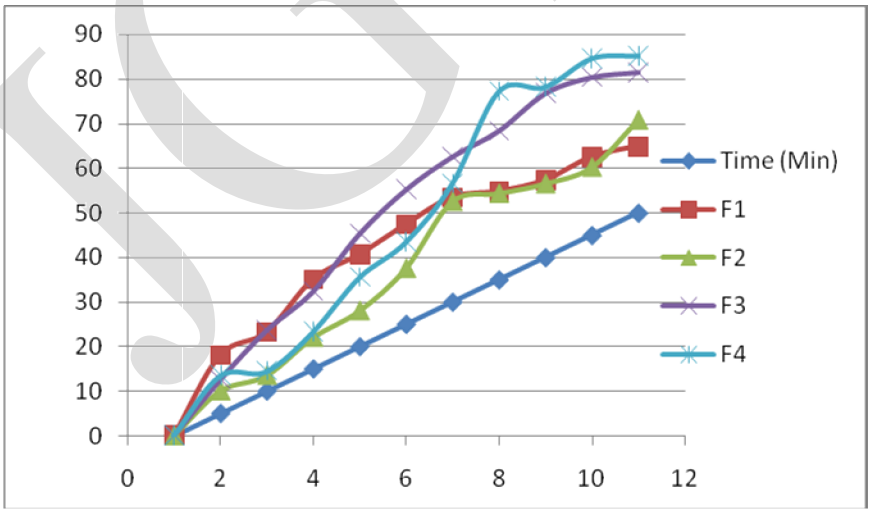

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TABLE: 2 Dissolution characteristics of Paracetamol dispersible tablet formulation:

Formulation	K value	R value
F1	0.0239	0.9871
F2	0.0238	0.9825
F3	0.0349	0.9870
F4	0.0422	0.9722

GRAPH: 2 Dissolution characteristics of Paracetamol dispersible tablet formulation

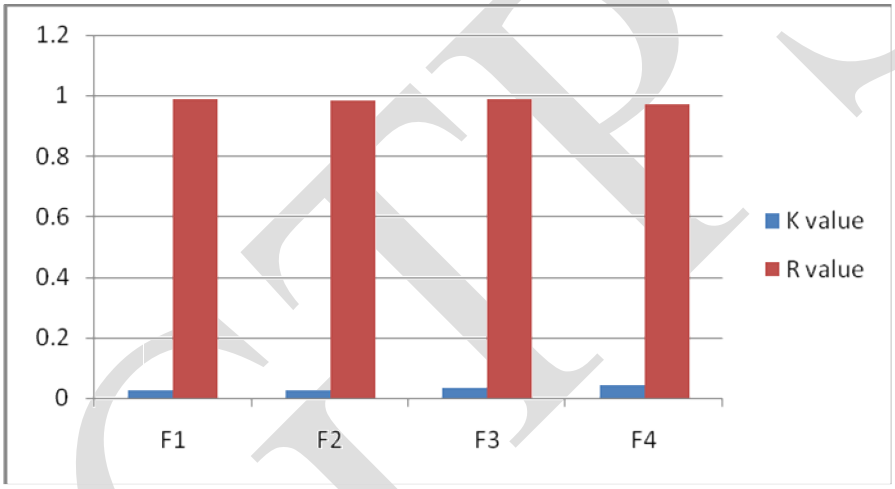

TABLE: 3 Hardness, Friability, Diameter & Thickness of the tablets formulation:

Formulation	Hardness(Kg/cm)	Friability	Diameter(mm)	Thickness(mm)
F1	2.5%	0.4%	9.05	1.68
F2	3.4%	0.5%	9.06	1.84
F3	3.1%	0.75%	8.96	1.66
F4	3.5%	0.9%	9.04	1.78

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TABLE: 4 Disintegration and %Drug content of formulation:

Formulation	Disintegration	%Drug content
F1	4.9	98.6
F2	3.7	101.5
F3	2.5	96.7
F4	2.5	104.5

TABLE: 5 Weight variations of tablets of the formulation F1, F2, F3 and F4:

S.NO	Formulation-I		Formulation-II		Formulation-III		Formulation-IV	
	Weight of each tablet(mg)	Percentage deviation	Weight of each tablet (mg)	Percentage deviation	Weight of each tablet (mg)	Percentage deviation	Weight of each tablet (mg)	Percentage deviation
1	140	-5.6	154	4.5	150	2.3	152	-3.1
2	153	2.8	155	5.3	155	2.4	153	-2.6
3	148	-0.7	152	3.1	149	1.3	155	-1.8
4	152	3.4	156	3.7	160	1.9	152	2.2
5	150	-1.5	153	5.5	163	-3.1	150	3.1
6	155	2.4	150	3.8	162	4.1	149	2.9
7	153	3.5	149	-1.4	159	2.0	148	3.2
8	151	4.6	147	2.1	155	1.0	146	2.9
9	149	1.5	146	1.9	154	3.9	145	1.0

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RESULT AND DISCUSSION:

The main objective of the study is to prepare the Paracetamol dispersible tablets. Paracetamol is having poor aqueous solubility. To improve its dissolution rate, various disintegrating agents' i.e. Potato starch and Primogel and different hydrophobic polymers such as HPMC-4000 &PVP were employed.

At first two formulations (F1&F2) were prepared by using Potato starch (10%), 5% as inter

granular disintegrating agent [9] and 5% as extra granular disintegrating agent .and F2 was prepared by using Primogel (5%) as extra granular disintegrating agent. both F1 & F2 are prepared by wet granulation method by using the same solvent ethyl alcohol as granulating fluid. and remaining excipients that is PVP (2%) as binder, Magnesium sterate (2%), Talc-(2%) were common[8]. After dissolution study it was revealed that Primogel used formulation F2 was showing better release of drug than potato starch used formulation F1.

Later solid dispersion of Paracetamol and hydrophilic polymer such as HPMC-4000, PVP were prepared in the same ratio 10:1 were prepared by physical mixing.

Then the resultant mixtures were subjected to granulation by using same wet granulation method and Primogel (5%) as extra granular disintegrating agent in both the formulations F3&F4 respectively. All the remaining process was same as explained above for the preparation of tablets. The dissolution study revealed that among these two formulations, F4 shows better release of drug than F3.

Finally it was concluded that formulation F4 in which Primogel (5%) used as extra disintegrating agents, solid dispersion of Paracetamol with PVP was made, showed the better release of the drug than other three formulations F1, F2, F3.

DISSOLUTION RATE: **F1<F2<F3<F4:**

The prepared formulations were passed the evaluation test that is weight variations, Percentage drug content, and disintegration, Uniformity of dispersion, Hardness & friability as per I.P Limits.[10]

CONCLUSION:

When compared to potato starch, the Primogel is showing better increase in rate of dissolution of prepared tablets. Out of those three formulations F2, F3 and F4 in which Primogel (5%) used as extra disintegrating agents was used.F4 was

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showing better increase in rate of dissolution of drug.F4 was prepared by solid dispersion of Paracetamol with PVP.

First order rate constant values: K2<K3<K4

Regression Coefficient values: R2<R3<R4

REFERENCES:

1. Herbert .Lieberman, Lachman Joseph L. Kanig*; Theory and Practice of Industrial Pharmacy* : *Leon*, Second edition,1976,p.293-298,326,330.

2. *Howard C, Ansel, Loyd V, Allen, Jr.Nichlas.G.Popovich, Pharmaceutical Dosage Forms* and Drug Delivery Systems, Sixth edition, 1985, Page: 193-196.

3. *British Pharmacopedia*, Published on the recommendation of the medicines commission pursuant to the medicines act 1968, volume 2, 2002.

4. Indurwade N.H., Ralyagaru T.H., Nakhat P.D., Navel approach-fast dissolving tablets, *Indian drugs*, August 2002.

5. Herbert A. Lieberman, Lachman and J.B Schwartz , *Pharmaceutical Dosage Forms Tablets* ,Volume.1,Second edition,MarcelDekkar,Inc,New Yark.1990 P.137-149.

6.*Brahmankar, D.M*, Sunil B Jaiswal, Text book of *Biopharmaceutics* and Pharmacokinetics, First edition,M.K.Jain,Vallabh Prakash,1997,p.42-43.

7. Alfred Martin, *Physical pharmacy*, 4th edition, B.L.Waverly Pvt.ltd., New Delhi,1999, Page;.442-443.

8. Herbert A. Lieberman, Lachman and J.B Schwartz Pharmaceutical dosage forms tablets, volume 3, second edition, and page: 500-501.

9. CIMS-65, volume.22, no.2, April-June 1999.

10. Indian Pharmacopiea, Published by the controller of publications, Delhi, Volume.1, 4th edition, 1996.

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