COMPARATIVE IN-VITRO EVALUATION OF FIVE DIFFERENT BRANDS OF DICYCLOMINE.HCL TABLETS

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ABSTRACT: The objective of current study is comparative in-vitro evaluation of five different brands of dicyclomine.hcl tablets. The chemical qualities of dicyclomine hydrochloride tablets marketed in India were assured and are independent of the drug's country of origin. The dissolution profile of the different brands of dicyclomine hydrochloride tablets revealed poor drug release. In vitro dissolution studies help in predicting biological drug release pattern in terms of rate and extent of release. No universal dissolution tests has been designed that gives the same rank order for in vitro dissolution and in vivo bioavailability. The present study showed that the weight uniformity, hardness, friability, disintegration time, absolute drug content, melting point, dissolution rate and anticholinergics activity of the five brands were determined using official method as applicable. The five brands passed the uniformity of weight test with the range of 0.351-0.676g, hardness test with range of 4.00- 10 kgF, friability test with range of 0.146-0.268%, absolute drug content a range of 98.82-107.02% and melting point tests and conformed with pharmacopeia specifications. The brands A,B,C and D and E showed appreciable activity against the test organism. All 5 brands of dicyclomine hydrochloride passed their test according to the criteria of Indian pharmacopeia.

KEYWORDS: Disintegration, Dissolution, Friability, Medicaments, Drug.

INTRODUCTION:

Dicyclomine oral tablet is a prescription medicine. It's available as a brand-name Bentyl drug. It is available as a generic drug. Generic drugs usually cost less than that.. Dicyclomine also comes as a capsule or solution that you take by mouth and by injection. The injection is given only by a health care provider in a clinic. Dicyclomine is an anticholinergic drug used to relax the smooth muscles of the intestines. It's duration of action is not especially long as it is usually taken 4 times daily with individual doses of 20-40mg orally or

10-20mg by intramuscular injection.6 Dicyclomine should not beadministered intravenously.

Because oral administration of drug is simple, convenient and safe, it is the most frequently used route. At least 90% of drug used to produce systemic effects are administered orally 1- 4.Immediate release tablet Immediate release tablets are those which disintegrate rapidly and get dissolved to release the medicaments. The term "release" includes the provision (or presentation) of drug from the formulation to the gastrointestinal tract, to body tissues and/or into systemic circulation. Tablet is the mostpopular among all dosage forms existing today because of its convenience of self- administration, compactness and easy manufacturing; however in many cases immediateonset of action is required than conventionaltherapy.

To overcome these drawbacks, immediate release pharmaceutical dosage form has emerged as alternative oral dosage forms. There are novel types of dosage forms that act very quickly after administration. The basic approach used in development tablets is the use of superdisintegrants like Cross linked carboxymelhylcellulose (Croscarmeliose), Sodium starch glycolate (Primogel, Explotab), Polyvinylpyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet after administration.

The treatment of smooth muscle spasm of the gastrointestinal tract an antispasmodic drug Dicyclomine HCl is widely used. It is rapidly absorbed orally but undergoes extensive first pass Metabolism.

So the present study aimed at developing mouth-melt tablets of Dicyclomine HCl using natural superdisintegrants to reduce first pass metabolism and to increase the

Bioavailability of drug which may show faster onset of action in relieving spasms of the gastrointestinal tractas compared to conventional tablet dosage form.Superdisintegrants by water absorption andswelling in the formulations exhibits faster disintegration, promotes wettability & dispersibility through increased wetted surface by providing faster disintegration and dissolution Recently, several countries have recorded a surge in recreational offer and use of pharmaceutical preparations containing synthetic cholinolytics for unregulated purposes, their abuse and "non-medical" use are mani- fested by a variety of mental and somatic disorders, behavioural disorders, social degradation One of these drugs is dicyclomine which has been a well-known drug of the grey marketfor quite a long time. However, it has recently been on the wave of interest in pharmacy substances that there has been a surge in its recreational popularity in the CIS countries,Eastern Europe, and the USA. Dicyclomine is used as an independent object of consumption, and as an adulterating agent of other more expensive psychoactive products Dicyclomine as a medicinal substance has cholinolytic, myotropic and antispasmodic effects, eliminates spasms of the smooth muscles of the gastrointestinaltract and reduces the pain syndrome caused by it. In therapeutic doses, it has a weak effect on the central nervous system, while in toxic doses it causes the development ofbright visual (less often auditory) hallucinations Dicyclomine is also included in the combined drug "Trigan D" containing 500 mg of paracetamol and 20 mg of dicyclomine hydrochloride. If 1–2 tablets are prescribed for

therapeutic purposesdepending on the severity of pain, 1–4 times a day, then drug addicts take this drug in an amount of more than 5 tablets at a time. In thiscase, there may be a pronounced psychomotor agitation, delusional disorders and euphoria accompanied by visual hallucinations.

MATERIALS AND METHODS:

MATERIALS:

Five different brand of dicyclomine. Hcl purchased from medical store and done their evaluation for quality purpose.

METHODS:

Disintegration test: Disintegration of dicyclomine hydrochloride tablets occurred within 5 minutes in each buffer solution and was unaffected by pH. At pH 2 and 3, dissolution of dicyclomine hydrochloride was greater than 85% complete after five minutes, and all dicyclomine hydrochloride had dissolved after 30 minutes. The effect of pH on the in vitro disintegration, dissolution, and solubility of dicyclomine hydrochloride tablets was studied One 250mg dicyclomine hydrochloride tablet was added to each of five different buffer solutions having pH values of 2 to 6;900 ml of each solution containing the dicyclomine hydrochloride was placed in a stationary basket dissolution device and stirred at 500 rpm at 37 degrees C for 60 minutes. Single 1-ml samples of each solution were obtained at 1,3, and 5 minutes after addition of the drug, and then every 5 minutes for the duration of the sampling period. To determine how quickly the tablets break down into smaller particles when exposed to specific conditions, mimicking the digestive system. According to IP the disintegration time of tablet is 15 minute.

Dissolution test: Dissolution is the process where a solute in gaseous, liquid, or solid phase dissolves in a solvent to form a solution. The veego tablet dissolution apparatus was used. The tablet was placed in a wire-meshbasket suspended in a dissolution medium of 500 ml of 0.1N HCl maintained at 37 ± 1O C in a water bath. The wire-mesh basket was rotated at a speed of 50 rpm and the experiment allowed to run for 60 minutes for each tablet tested. The stirrer was maintained at a constant speed. At predetermined time interval, 5 ml samples were withdrawn from the beaker and the volume immediately replaced with 5ml of 0.1NHCl. The withdrawn samples were diluted in a 50-ml volumetric flask and analyzed for dicyclomine hydrochloride contents at 235 nm using a UV-Vis 2102 PC spectrophotometer. The concentration of the active ingredient was then obtained from the standard Beer Lambert's plot. To assess how quickly and effectively the tablets dissolve in simulated gastric orintestinal fluids. This is important for drug absorption. According to IP dissolution time of film coated tablet dissolve with in 30 minutes, & other coated tablet dissolve within 60 minutes.

Uniformity of weight test: Five different tablets are selected from each brand, were weighed individually and collectively using an analytical weighing balance. The mean weights, as well as the deviations

(standard error of mean), of the individual tablets from the mean weight werecalculated.

Hardness test (crushing strength): Five tablets were randomly selected from each brand and their hardness determined using the Mosanto Stokes hardness tester. Each tablet was placed between the spindle and anvil and pressure applied by turning the knob sufficiently to hold the tablet in position. The pointer on the scale was adjusted to zero reading and pressure gradually and steadily increased until the tablet breaks. The pointer reading from the scale was taken as the pressure required to break the tablet. The above procedure was repeated for the five different brands of dicyclomine hydrochloride tablets.

Friability test: Five tablets from each brand of dicyclomine hydrochloride tablets were de-dusted,weighed and subjected to vibration and shock in a Roche Friabilator rotating at 25 rpm for 5 minutes. Thereafter, they were de-dusted, reweighed and the percentage loss in weightcalculated using the equation :

Percentage friability = loss in weight/initial weight x 100.

Friability calculation formula :

% weight loss = W2-W1/W1× **100**Where,

W1= initial weight and W2= final weight

RESULT & DISCUSSION:

DISINTEGRATION TEST:

Name	Times
Almefkem spas (250mg)	2.0 minute.
Cyclopam (500mg)	1.41 minute.
Meftal spas (250mg)	27 second .
Minta- M (250mg)	27 second
Spasmonil (325mg)	30 second

DISSOLUTION TEST:

Name	Solution	Temperature	Time
Almefkemspas (250mg)	Buffer	37 ± 2^{o} c	16 .8 minutes.
Cyclopam(500mg)	Buffer	37 ± 2^{o} c	32 minutes.
Meftal spas (250mg)	Buffer	37 ± 2^{o} c	16.2 minutes.
Minta-M (250mg)	Buffer	37 ± 2^{o} c	15.6 minutes.
Spasmonil (325mg)	Buffer	37 ± 2^{o} c	33.4minutes.

UNIFORMITY OF CONTENT TEST:

Name	Weight
Almefkem spas (250mg)	0.5 gm
Cyclopam (500mg)	0.7 gm
Meftal spas (250mg)	0.5 gm
Minta-M (250mg)	0.5 gm
Spasmonil (325mg)	0.6 gm

HARDNESS TEST:

Name	Breaking weight
Almefkem spas (250mg)	8 kgF.
Cyclopam (500mg)	10 kgF
Meftal spas (250mg)	7 kgF
Minta-M (250mg)	7 kgF
Spasmonil (325mg)	4 kgF

FRIABILITY TEST

Name	Initial weight (w1)	Final weight(w2)	Friability %
Almefkem spas (250mg)	0.5 gm	0.4 gm	0.5 %
Cyclopam (500mg)	0.7 gm	0.6 gm	0.52 %
Meftal spas (250mg)	0.5 gm	0.3 gm	0.6 %
Minta-M (250mg)	0.5 gm	0.3 gm	0.77 %
Spasmonil (325mg)	0.6 gm	0.5 gm	0.8 %

SUMMARY AND CONCLUSION

The dicyclomine hydrochloride were all circular in shape and had colours that varied between white and offwhite colour. The identity profiles of the different brands of dicyclomine hydrochloride tablets marketed in India are presented in Table. The five brands of dicyclomine hydrochloride tablets passed the weight uniformity test for compressed uncoated tablets (Lund, 1994). Tablet weight variations are attributed to various formulation factors which are dependent on the manufacturer.

The hardness and friability tests results revealed that the five brands complied with the crushing strength (4.0- 10 kgF) and friability (0.5-1.0% loss in weight) specifications (British Pharmacopoeia, 1998; Ofoefule, 2002; USP, 2005). According to of oefule, 2002, friability is a measure of the resistance of tablets and granules formulations of pharmaceutical products to abrasion. The results confirm that the dicyclomine hydrochloride brands could withstand the stress of handling and transportation. The results of the disintegration time (DT) test showed that the five brands of dicyclomine hydrochloride tablets had

disintegration times ranging between 0.27 and 02.0 minutes.

The test tablets are considered to have satisfactory DT values since the obtained valuesare in agreement with the mean disintegration time specification for uncoated tablets which should not exceed 15 minutes (British Pharmacopoeia, 2004).

In the context of tablet technology, disintegration implies penetration of the tablet by an aqueous liquid, disruption of internal bonds and subsequent breakdown of the tablet.

Factors that can affect disintegration time of the tablets include the rate at which a liquidpenetrates a tablet, the nature and method of incorporation of lubricants, the action of disintegrants, and the degree of compaction and reduction of inter-particle bondstrength in the presence of water (Rawlins, 1970), All the brands of dicyclomine hydrochloride tablet had active ingredient which fell within the USP, 2004 acceptablelimit of 90 110 %.

The chemical qualities of dicyclomine hydrochloride tablets marketed in India were assured and are independent of the drug's country of origin. The dissolution profile of the different brands of dicyclomine hydrochloride tabletsrevealed poor drug release.

In vitro dissolution studies help in predicting biological drug release pattern in terms of rate and extent of release. No universal dissolution tests has been designed that gives the same rank order for in vitro dissolution and in vivo bioavailability. The present study showed that the weight uniformity, hardness, friability, disintegration time, absolute drug content, melting point, dissolution rate and anticholinergics activityof the five brands were determined using official method as applicable.

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Approximately one-third of the patients need quick therapeutic action of drug, resulting in poor compliance with conventional drug therapy which leads to reduced overall therapy effectiveness. A new dosage form, the immediate release pharmaceutical form has been developed which offers the combined advantages of ease of dosing and convenience of dosing. These tablets are designed to release the medicaments with an enhanced rate. Mefenamic acid and Dicyclomine HCl combination therapy is widely used in market. This combination not only controls pain very effectively but also reducebodily spasm which commonly arises from menstruation or colic spasm. In market theconventional doage form of Mefenamic acid and Dicyclomine HCl is available but it gives slow onset of action. In present study the Immediate release tablet of Mefenamicacid and Dicyclomine HCl were prepared by direct compression method using

Crospovidone and Croscarmellose sodium as superdisintegrants. Mefenamic acid and Dicyclomine HCl was initially characterized for its preliminary studies such as organoleptic properties, melting point, solubility, UV Spectroscopy and FTIR studies and also drug-excipients compatibility was confirmed by FTIR. Optimization of Immediate release tablet was carried out by in vitro drug release at 16 min., disintegration time. The nine formulations prepared were subjected to physical evaluation parameters like hardness, thickness, weight uniformity, wetting time, drug content uniformity, Water absorption ratio, in vitro drug release, disintegration time.

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