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FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLET OF DOMEPERIDONE MALEATE AND COMPARISION WITH MARKETED FORMULATION.

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ABSTRACT ; Orodispersible drug delivery systems are used to improve how much of a drug is absorbed by the body and to make it easier for patients to take their medication.

Orodispersible tablets, a new type of medicine, quickly break down in the mouth (within 1-3 minutes) when taken orally, without needing to be chewed or swallowed with water. Compared to regular tablets and capsules, orodispersible tablets (ODT) have gained attention over the past three decades because they offer better patient compliance, increased solubility, and stability.

Orodispersible tablets have the special characteristic of rapidly disintegrating within seconds when placed on the tongue, as they mainly consist of medicinal substances in solid form.

This innovative ODT technology improves the overall treatment experience for patients, especially those with difficulties swallowing, such as children, older adults, and individuals with psychiatric conditions.

This advancement in technology has motivated the academic and industry sectors to develop new ways to formulate and evaluate orally disintegrating medications that will be beneficial for future drug candidates.

Keywords: Orodispersible, Tablet, Domperidone ,Orodispersible drug delivery system.

1 INTRODUCTION[1]

Direct ingestion is intended in most pharmaceutical dosage forms which are formulated for oral administration. The oral route is the best or convenient way of drug administration for patients andthis way is used by most of the therapeutic agents for producing effects of the oral route. A term used by the "European Pharmacopoeia" orodispersible tablet, this table disperses in the mouth within 3 seconds before swallowing it.

1.1 Oro Dispersible Tablets (ODTs)

Oral dispersible tablets (ODTs) are the novel dosage form which quicklydisintegrates in the mouth(1-3 min) without chewing upon oral administration and without the need of water, different other conventional oral solid dosage form. The best time for an orodispersible tablet to get separate is measured to be fewer than a minute.

Mostly the degeneration times vary from 5 to 30 seconds and are prepared to recount; direct compression, solid dispersion, lyophilization or molding techniques.

ODTs are recognized by the addition of super disintegrants alike cross-linked cellulose imitative; carboxymethyl cellulose, sodium starch glycolate,polyvinylpyrrolidone, which provides rush breakdown when gets in exchange with water or salivary secretions.Bioavailability of drugs may rise due to oral and pregastric.

1.2 Ideal Properties of Orodispersible Tablets[1]

- Not require water to absorb and should dissolve or disintegrate in the mouth within a few seconds.
- High drug loading.
- Have a pleasant mouthfeel.
- Be agreeable with taste masking and other excipients.
- Mainly in the condition of insoluble and hydrophobic drugs increase the bioavailability, due torapid disintegration and dissolution of these tablets.

1.3 Limitations of Orodispersible Tablets (Odts)[2]

- Many times the soluble diluents used for formulating the ODTs might give hygroscopic dosagewhich may lead to stability issues.
- The tablets are unpleasant to taste and/or roughness in the mouth if not formulated properly.
- Specialized packing might be required for hygroscopic and light-sensitive drugs.
- Precautions to be taken while administering immediately after removing from the pack.
- Light sensitive drugs, ODTs may not be suitable as no option for film coating.

1.4 Advantage of Orodispersible Tablets (Odts)[3]

- Improved stability.
- Suitable for controlled/sustained Offers improved compliance andconvenience to patients and prescribers.
- It improves patient adherence and reduces the development of resistance in the case ofantimicrobials.
- Simplifies the logistics of procurement and distribution.
- For Rapid drug delivery, ODTs are considered to be preferred dosage form.
- The drug is released quickly from this dosage form and gets dissolve in GIT tract without gettinginto the stomach, increased bioavailability can be achieved.
- ODTs are very convenient for administering to various classes of patients from disabled, travelersand busy people, who do not always have access to water.
- Some drugs are absorbed from the pharynx and esophagus as the saliva passes down into thestomach; in such cases, the bioavailability of drugs is increase.
- No water needed.
- No chewing needs.
- Better taste.
- release actives.
- Allow high drug loading.

1.5 Disadvantage Of Orodispersible Tablets(ODTS)[4]

- Rapid drug therapy intervention is not possible.
- Sometimes may require more frequency of administration.
- Dose dumping may occur.
- Reduced potential for accurate dose adjustment.
- For properly stabilization and safety of the stable product, ODTrequires special packaging.
- Usually have insufficient mechanical strength. Hence, carefulhandling is required.
- Leave unpleasant taste and/or grittiness in the mouth if notformatted properly.

1.6 Some Examples Of Recently Prepared Orodispersible Tablets

Ofloxacin-
Taste masked microspheres of the ofloxacin were prepared as a using Eudragit and orodispersibletablets of the formulated microspheres were using the nature of the superdisintegrant.

Nimesulide -

Orodispersible tablets were then completed using locust bean gum as a natural of thesuperdisintegrant.

Cetirizine dihydrochloride -
Tablets were organized using cetirizine along with camphor and mannitol in different quantity.

Pheniramine maleate -Effervescent method.

Diazepam –
ODTs were organized using different types of superdisintegrants at changed concentration usingwet granulation and direct compression methods.

Valsartan -
Tablets were arranged by freeze-drying method.

Ondansetron HCl -
Direct compression technique.

Roxithromycin -
ODTs were arranged using modified polysaccharides as fast disintegrating excipients.

Indomethacin -
The tablets were complete by the non- aqueous wet granulation method with superdisintegrantincluded both of the intragranularly and extragranularly.

1.7 Various technologies used in the manufacture of orodispersible tablets consist of

- Direct compression.
- Sublimation.
- Freeze-drying or lyophilization.
- Tablet Molding.
- Spray drying.
- Cotton candy process.
- Mass extrusion.
- Phase transition.
- Nanonization.

- Fast dissolving films.

3 AIM AND OBJECTIVE[2]

1.8 AIM

Formulation and evaluation of orodispersible Tablets of domeperidone maleate and comparisonwith marketed formulation.

1.9 OBJECTIVE

1. To improve patient compliance.
2. To increase bioavailability.
3. To enhance stability.
4. To formulate oro dispersible tablet having less disintegration time.
5. To compare the drug release profile of formulated and marketed tablet.

2 PLAN OF WORK

1) Literature survey.
2) Selection and procurement of excipients.
3) Formulation of Orodispersible tablet of domeperidone.
4) Evaluation of formulated tablet of domeperidone.

a) Standard calibration of pure drug.
b) Dissolution of formulated tablet.
c) Comparison of drug release profile of formulated tablet and marketed tablet of domeperidone.

3 LITERATURE REVIEW

Aithal.k. et al.[5] 2006, developed once daily fast dissolving tablet of granisetron HCl by direct compression method using super disintegrating agent. Formulation containing cross povidone and croscarmellose sodium shows shortest disintegrating time.

T.V.Rao et al.[6] 2008,worked on the formulation and evaluation of Cefodroxil dispersible tablets by direct compression technique using super disintegrating such as crosspovidone, croscarmellose sodium, sodium starch glycolate. The tablets were evaluated for hardness, weight variation, friability, wetting time disintegration time and in vitro dissolution study.

Mallikarjuna setty et al.[7] 2008, designed the fast dispersible aceclofenac tablet and effect of functionality of super disintegrating agents. Aceclofenac fast dispersible tablet have been preparedby direct compression method. Effect of superdisintegrants such as croscarmellose sodium, sodiumstarch glycolate and crosspovidone on wetting time, disintegration time od drug content in vitro release has been studied.

Stoltenberg et al (2011)[8] developed orally disintegrating mini-tablets as a suitable dosage form for pediatric patients.The suitability of five commercially available ready-to-use tablet excipients, Ludiflash, Parteck ODT, Pearlitol Flash, Pharmaburst 500 and Prosolve ODT,to be directly compressed into tablets, with 2 mm in diameter, was examined.

Johnny Edward Aguilar-Diaz et al (2012)[9] studied a new innovative tool for pharmaceutical preformulation to predict whether a disintegrants excipients or mixture of powder containing API +excipients is suitable to obtain a orodispersible tablets by direct compression or not.The IGCF index is composed of six main factor which indicates the aptitude to be compressed by direct compressionand at the same time indicates wheter these tablets are suitable to be used as a orodispersible tablet(disintegration lower than 3 min).

EXPERIMENTAL WORK

3.1 Formulation Of Tablets Of Domeperidone :-

For formulation of tablets of domeperidone 10 mg,there is need of various components like drug,super disintegrants,sugar,additive and other excipients:

1) Drug – Domeperidone maleate.
2) Super Disintegrants – Sodium starch glycolate (SSG), cross povidone (CP),Cross carmellous sodium (CCS), cross cellulose(CC), etc.
3) Sugar – Mannitol,saccharin.
4) Others excipients – Talc,magnesium stearate.

For the formulation of tablets batches we have used direct compression method:

Direct compression: Direct compression characterizes the simplest and most cost-effective tablet manufacturing technique. This method can now be practical to the research of ODT because of theaccessibility of enhanced excipients mostly super disintegrants and sugar-based excipients.The mixture to be compressed must have suitable flow of the properties and cohere under pressure thus assembly pretreatment as the wet granulation is excessive.Limited drugs can be directly compressedinto tablets of standard quality. The disintegrant addition technology is cost-effective and easy to implement at the industrial level.

There are total of five formulations using different super disintegrants

Table No. 1 :-composition of different batches of orodispersible tablet

Sr.No	**Ingredients**	F1	F2	F3	F4
1	Drug	10 mg	10 mg	10 mg	10 mg
2	Superdisintegrants	10 mg	10 mg	10 mg	10 mg
3	Sweetening agent	75 mg	75 mg	75 mg	75 mg
4	MagnessiumStereate	3 mg	3 mg	3 mg	3 mg
5	Talc	2 mg	2 mg	2 mg	2 mg

After formulation of batches we have to perform dissolution testing for all five batches.

3.2 Preparation Of Phosphate Buffer pH 6.8 :-

1) Preparation of 0.2M sodium hydroxide: Dissolve about 8 g of sodium hydroxide in sufficient quantity of distilled water made up to 1000 ml with distilled water.
2) Preparation of 0.2M potassium dihydrogen phosphate: Dissolve potassium dihydrogen phosphateabout 27.218 g in sufficient quantity of distilled water and made up to 1000 ml with distilled water.3)Preparation of phosphate buffer pH 6.8: Take about 50 ml of potassium dihydrogen phosphate in200 ml volumetric flask and add 22.4 ml of 0.2M sodium hydroxide and made up to 200 ml with distilled water. Check the pH of resulting solution and adjust to pH 6.8 by using 0.2M sodium hydroxide solution.

3.3 Dissolution Testing :-

Fig 1:- Dissolution apparatus

1) In the apparatus the buffer is placed and dissolution is performed bymaintaining sink condition.
2) Dissolution is performed by comparing 2 different batch tabs at a time900 ml of buffer is placed in one glass for dissolution.
3) As tablets are fast disintegration,sample is withdrawn after 2 min interval.
4) 4ml of sample is withdrawn after each 2 min for each batch and sink is maintained by addition of4 ml buffer of 6.8 pH.
5) This procedure is performed repeteadly for all samples(at least 3 samples for each batch).6)Same process is done for the marketed preparation.

4 EVALUATION OF ORODISPERSIBLE TABLETS

4.1 Evaluation By UV -visible spectrophotometer :-

Samples obtained from dissolution testing were analysed by UV -visible spectrophotometer at284nm after suitable dilution and filtration.

7.3 Determination of % drug release from std calibration curve-

Table No.2 :- Drug concentration obtained from std calibration curve

Time	F1	F2	F3	F4	F5
2 min	0.75 µg	3.2 µg	7.25 µg	6.5 µg	3.2 µg
4 min	1.15 µg	3.7 µg	6.5 µg	5.5 µg	5.3 µg
6 min	1 µg	3 µg	7.25 µg	5.75 µg	8.4 µg

In the graph between absorbance vs concentration for total of 6 points more than 4 points are aligned,it means the reading of absorbance are so accurate and the buffer is also of very standardize quality.

From above graphs we get the values for drug released on the line intersection points.From which we can calculate the percentage drug release below from the formula.

7.3 Scanning of pure drug by UV spectrophotometer :-

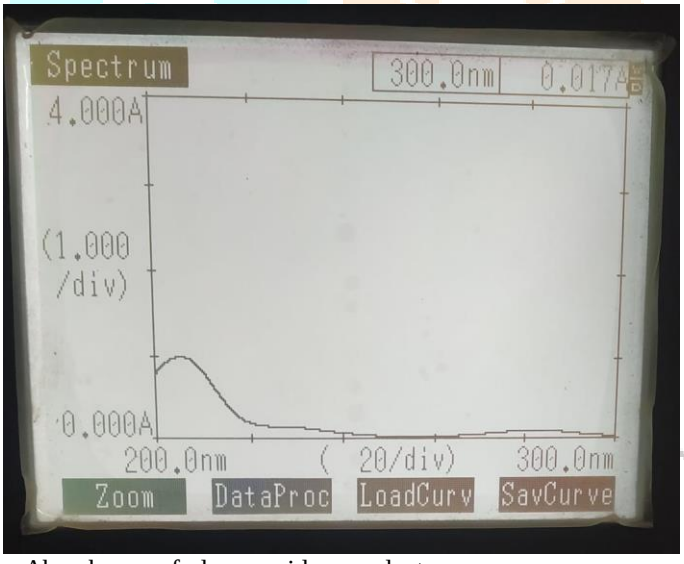

Fig 2:- Absorbance of domeperidone maleate

7.5 Standard Calibration curve of Domperidone maleate

Standard calibration of pure drug is performed to get the drug release profile. Pure drug is mixed with the equal amount of buffer to get definite concentration.Hence the dilution factor is 1 for the drug. i.e 50 mg of drug in 50 ml of buffer.
But if drug is not soluble in buffer we can use alcohol or ether like propylene glycol or isopropylalcohol.
After dilution samples are taken from the 100 ml of stock solution as follows.0.5ml, 1.0ml, 1.5ml, 2.0ml, 2.5ml, 3.0ml.
And mixed with 100 ml of buffer and then absorbance is evaluated. Table No.3 :- Standard calibration of pure drug (domeperidone maleate).

Sr.No	Volume of stocksolution	Concentration in µg/ml	Absorbance at 284 nm
1	0.5 ml	5 µg/ml	0.097
2	1.0 ml	10 µg/ml	0.199
3	1.5 ml	15 µg/ml	0.296
4	2.0 ml	20 µg/ml	0.397
5	2.5 ml	25 µg/ml	0.476
6	3.0 ml	30 µg/ml	0.573

7.6 Drug Release Profile :-

Drug is released in continuous manner from the solution. It is determined from std calibration curve.

7.7 Formula For Percentage Drug Release:-

% DR =[X × 900 × 2 ÷ 10 × 1000] × 100

7.8 Percentage (%) Drug Release :-

Table No.4 :- Data for all the batches of percentage drug release.

Time	F1	F2	F3	F4	F5
2 min	13.5 %	58.5 %	130 %	117 %	57.6 %
4 min	20.7 %	67.5 %	117 %	99 %	95.4 %
6 min	18 %	54 %	130 %	103.5 %	151.2 %

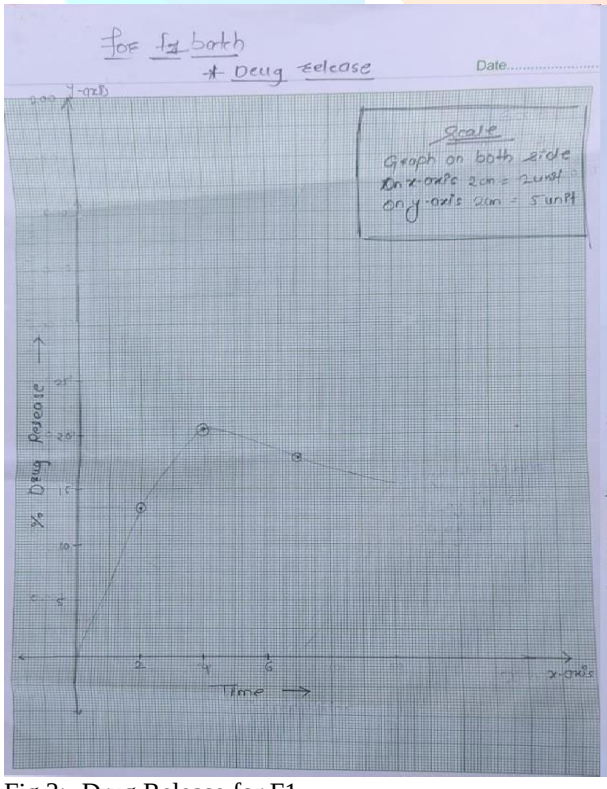

Fig 3:- Drug Release for F1

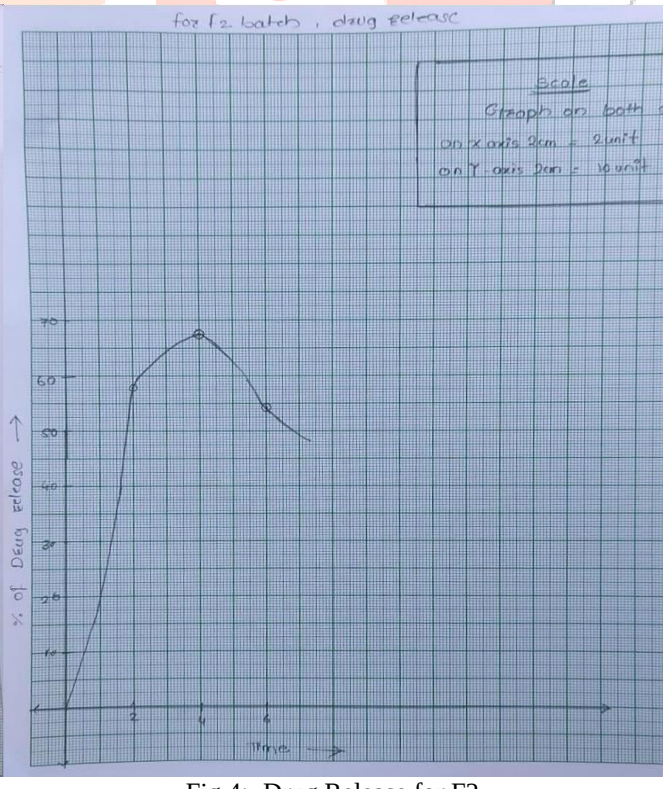

Fig 4:- Drug Release for F2

Drug release profile for batch F1,

The graph is taking shift towards x-axis means as time passes drug get to maximum release,but afterachieving certain level then drug release get to lower it means it bend downward.

For 4th minute it shows maximum drug release of 20.7 %.

Drug release profile for batch F2,

The graph is taking shift towards x-axis means as time passes drug get to maximum release,but afterachieving certain level then drug release get to lower it means it bend downward.

For 4th minute it shows maximum drug release of 67.5 %.

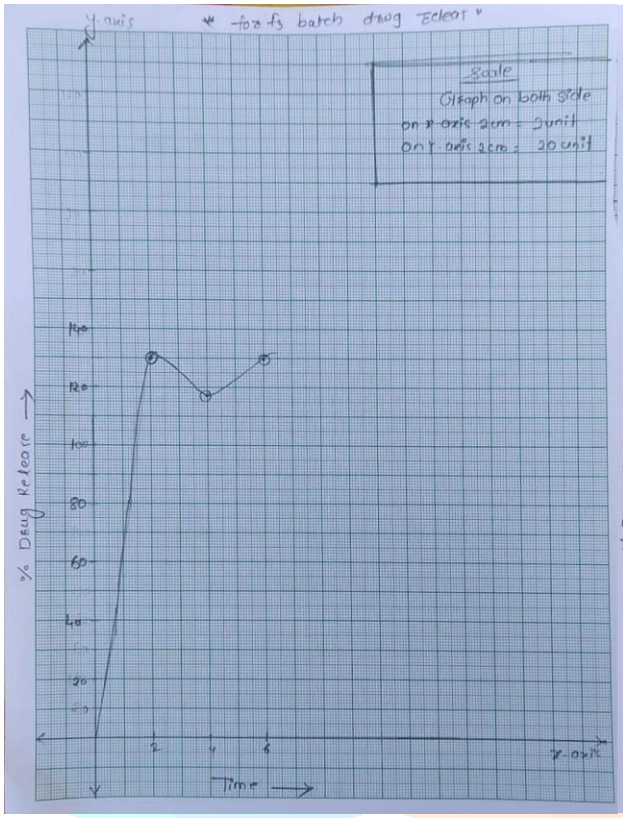

Fig 5:- Drug Release for F3

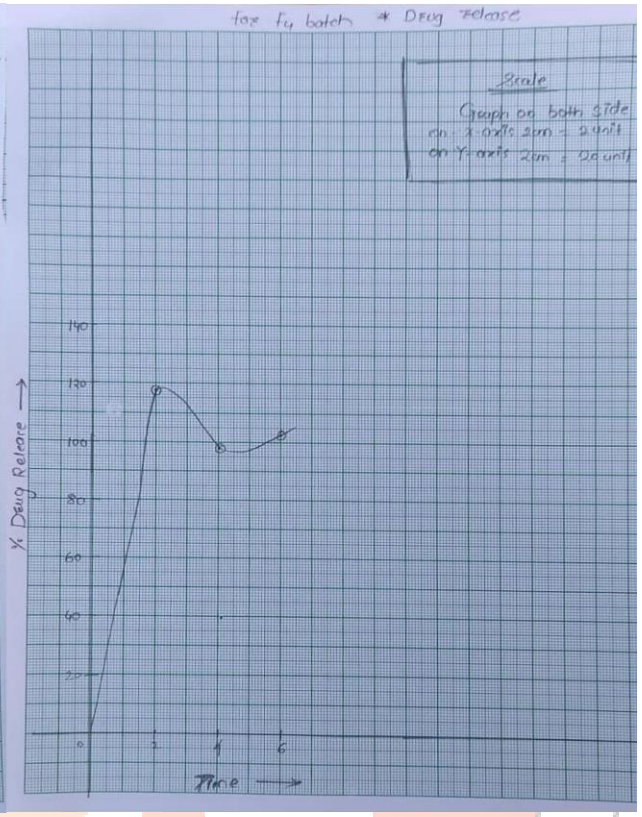

Fig 6:- Drug Release for F4

Drug release profile for batch F3,

The graph is taking shift towards x-axis means as time passes drug get to maximum release,but afterachieving certain level then drug release get to lower it means it bend downward.
But in this particular case the graph goes down in 4th minute but then again goes up to maximum %drug release.

For 2nd and 6th minute it shows maximum drug release of 130 %.

Drug release profile for batch F4,

The graph is taking shift towards x-axis means as time passes drug get to maximum release,but afterachieving certain level then drug release get to lower it means it bend downward.
But in this case the maximum drug release is at 4th and 6th minutes the drug shows lower % drugrelease.

For 2nd minute it shows maximum drug release of 117 %.

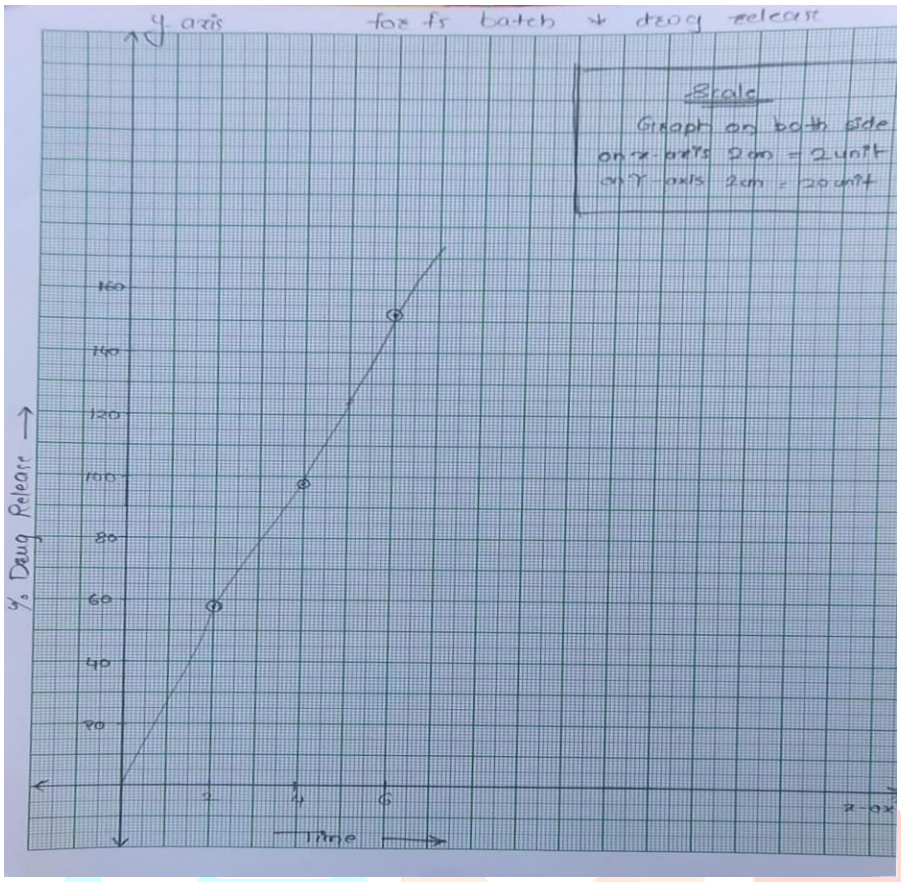

Fig 7:- Drug Release for F5

Drug release profile for batch F5,

The graph is going upwards as the time passes percentage drug release rate increases in a continuousmanner.
It is the drug release profile of the marketed preparation.
As compare to the other batches it shows very continuous % drug release.For 6th minute it shows maximum drug release of 151.2 %.

5 RESULT AND DISCUSSION

5.1 Observation For Dissolution :-

Different batches tablet shows different disintegration time as we used the different super-disintegrants.

The batch F1 tablet shows slower disintegration as compared to other batches of nearly between4 min - 5 min. It is relatively slower than others.

The batch F2 tablet shows faster disintegration as compared to F1 but slower than some othersnearly of 4.45 min.

The batch F3 tablet shows slower disintegration as compared to other batch F5 but faster than formertwo cases nearly of 3 min - 4 min.

The batch f4 tablet shows rapid disintegration as compared to other former batches of nearly of 2 min only. It is because we used mixture of disintegrants for formulation of tablets as compared otherin which only one is chosen.

F5 which is marketed preparation is shows rapid disintegration time of 1-2 minutes only.

For Drug % Release :-

F1 shows maximum percentage drug release of only 20.7 % only. **F2** shows maximum percentage drug release of only 67.5 % only. **F3** shows maximum percentage drug release of only 130 % only. **F4** shows maximum percentage drug release of only 117

% only. **F5** shows maximum percentage drug release of only 151.2 % on

8.2Optimization

From the above observations it is found that Dissolution study shows that the marketed and formulated tablet F4 are of same disintegration time that is of 1-2 minutes only so,
F4 and **F5** are having same disintegration profile.

Drug released profile shows that the **F3** and **F4** shows the highest percentage drug

9 CONCLUSION

Orodispersible tablets (ODTs) are innovative drug delivery systems and have potential advantages overconventional dosage forms, with their improved patient compliance, convenience, bioavailability and rapid onset of action . Though considerable research has been done in the formulation development and technologies for ODTs, more intensive investigations are to be carried out in this promising area to result in newer cost effective technologies and better products. The potential of dosage forms is promising because of the availability of new technologies combined with strong mark.

From the above discussion we can conclude that the formulated tablet **F3** and **F4** shows resemblancewith marketed preparation **F5**.

Hence crosspovidone and mixture of super disintegrants use tablet shows close resemblance with characterstics of the marketed tablet of domeperidone maleate.

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