



ISSN: 0975-766X  
CODEN: IJPTFI  
Review Article

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## EFFECT OF OSCIMUM BASILICUM ON FORMULATION AND EVALUATION OF RAPID DISINTEGRATING TABLET OF LAMOTRIGINE

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Received on 21-07-2012

Accepted on 04-08-2012

### Abstract

The main aim for performing this project is to increase the bioavailability of lamotrigine as well as its onset of action to control the seizures that occur during the epileptic attack. To serve this purpose we will use mucilage of *oscimum basilicum* as a natural superdisintegrant & later comparing it with different novel synthetic superdisintegrant. By preparing a rapid disintegrating tablet of lamotrigine, rapid action of same can be achieved easily.

As we know that superdisintegrant plays the major role in rapid disintegration of tablet, thus it is very important to select a right or correct superdisintegrant in all respect which fulfill its purpose without effecting other parameters of tablet formulation and gives quicker and better result, when the number of formulation with different combinations of superdisintegrants(Natural & Synthetic) will be made then it would become very easy to evaluate and get the formulation with maximum desirable results. Lamotrigine being a poorly water soluble drug, needs modification to make them water soluble.

### Introduction

Rapid Disintegrating Tablets are solid dosage forms containing medicinal substances which disintegrate rapidly, usually in a matter of seconds, when placed on the tongue. Many pharmaceutical dosages are administered in the form of pills, granules, powders, and liquids. Generally, a pill design is for swallowing intact or chewing to deliver a precise dosage of medication to patients. The pills, which include tablets and capsules, are able to retain their shapes under Moderate pressure. However, some patients, particularly pediatric and geriatric patients, have difficulty swallowing or

chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take these solid preparations due to a fear of choking. In order to assist these patients, several fast-dissolving drug delivery systems have been developed. Fast-dissolving drug delivery in recent years, a variety of improved methods for delivering drugs has been developed with the aim of improving performance, convenience and compliance. Rapid Disintegrating Tablets disintegrate and or dissolve rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate. When put on tongue, this tablet disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva. Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form. The advantage of orally disintegrating dosage forms are increasingly being recognized in both industry and academia.

Rapid Disintegrating Tablets, as a novel dosage form, have several characteristics to distinguish them from the more traditional dosage forms. Taste-masking is of critical importance in the formulation of an acceptable RAPID DISINTEGRATING TABLETS. Traditional tablet formulations generally do not address the issue of taste masking, because it is assumed that the dosage form will not dissolve until passing the oral cavity.

**List of rapid disintegrating tablets of lamotrigine Available in the Market.**

S.No.	Brand Name	API (in mgs)	Manufactured by
1	Lamepil	Lamotrigine (25, 50, 100)	Innova (Ipca)
2	Lemetec	Lamotrigine (5, 25, 50, 100)	Protec (Cipla)
3	Lamidus	Lamotrigine (25, 50, 100)	Zydus Neuro
4	Lamitor-DT	Lamotrigine (25, 50, 100)	Mind(Torrent)
5	Lyzin	Lamotrigine (25, 50, 100)	Pifer
6	Lametec DT	Lamotrigine (5, 25, 50, 100)	Protec (Cipla)

7	Lamidus Dispertab	Lamotrigine (25, 50, 100)	Zydus Neuro
8	Lamictal	Lamotrigine (5, 25, 50, 100)	GSK

### Significance of Rapid Disintegrating Tablets

- Convenience of administration and accurate dose as compared to liquids.
- No need of water to swallow the dosage form, which is highly convenient feature for patients who are travelling and do not have immediate access to water.
- Ease of administration to patients who refuse to swallow a tablet, such as pediatric, geriatric, mentally ill, disabled and uncooperative patients.
- Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach; in such cases bioavailability of drugs is increased.
- Good mouth feel property of RAPID DISINTEGRATING TABLETSs helps to change the psychology of medication as “bitter pill” particularly in pediatric patients.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Rapid dissolution of drug and absorption, which may produce rapid onset of action.

### Mechanism of Tablet Disintegration

The mechanism by which the tablets are broken into small pieces and then produce a homogeneous suspension is based on:

- Capillary action/ water wicking
- By swelling
- Air expansion /heat of wetting
- Due to disintegrating particle/particle repulsive forces
- Due to deformation
- Due to release of gases
- By enzymatic reaction

## Challenges In the formulation of Orally Disintegrating Tablets

### **a. Palatability**

It is a formidable challenge for formulation scientists to mask the taste of bitter tasting drugs selected for Oral disintegrating tablets. As most drugs are unpalatable, orally disintegrating drug delivery systems usually contain the medicament in a taste-masked form. Hence, taste-masking of the drugs becomes critical to patient compliance.

### **b. Mechanical strength**

In order to allow Rapid Disintegrating Tablets to disintegrate in the oral cavity, they are made of either very porous or soft molded matrices or compressed into tablets with very low compression force, which makes the tablets friable or brittle, and difficult to handle. Only few technologies can produce tablets that are sufficiently hard and durable to allow them to be packaged in multidose bottles.

### **c. Hygroscopicity / Moisture sensitivity**

Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need protection from humidity which calls for specialized product packaging.

### **d. Dose /Amount of drug**

The application of technologies used for Rapid Disintegrating Tablets is limited by the amount of drug that can be incorporated into each unit dose. Molecules requiring high doses present mainly three challenges to the development of fast dissolve dosage forms; a) taste masking of the active ingredient, b) mouth feel or grittiness and c) tablet size. These challenges are not unrelated because most drugs will require taste masking, the amount of taste masking materials used in different dosage forms will depend on the drugs degree of bitterness relative to its dose, which will in turn affect the final tablet size.

### **e. Aqueous solubility**

Water-soluble drugs pose various formulation challenges because they form eutectic mixtures, which result in freezing-point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting

structure during the sublimation process. Such collapse sometimes can be prevented by using various matrix forming excipients such as mannitol than can induce crystallinity and hence, impart rigidity to the amorphous composite.

#### **f. Size of tablet**

The degree of ease in taking a tablet depends on its size. It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was one larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve.

#### **g. The Drug Property**

Many drug properties could potentially affect the performance of fast dissolving tablets. For example, the solubility, crystal morphology, particle size and bulk density of a drug can affect the final tablet characteristics, such as tablet strength and disintegration.

#### **h. Mouth feel**

The RAPID DISINTEGRATING TABLETS should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the RAPID DISINTEGRATING TABLETS should be as small as possible. RAPID DISINTEGRATING TABLETS should leave minimal or no residue in mouth after oral administration. Moreover addition of flavors and cooling agents like menthol improve the mouth feel.

#### **i. Sensitivity to environmental conditions**

RAPID DISINTEGRATING TABLETS's generally should exhibit low sensitivity to environment conditions such as humidity and temperature as most of the materials used in an RAPID DISINTEGRATING TABLETS are meant to dissolve with minimum quantity of water.

### **ROLE OF SUPER-DISINTEGRANTS IN RAPID DISINTEGRATING TABLETS**

Superdisintegrant plays the major role in Rapid disintegrating tablet. The disintegration efficiency is based on the force-equivalent concept (the combined measurement of swelling force development and amount of water absorption). Superdisintegrants are generally used at a low level in the solid dosage form, typically 1 – 10 % by weight relative to the total weight of the dosage unit. Common disintegrants used are Croscarmellose sodium (Vivasol, Ac-Di-Sol), Crospovidone (Polyplasdone), Carmellose (NS-300), Carmellose calcium (ECG-505), Sodium starch glycolate (SSG)

Sharma Akansha\* et al. /International Journal Of Pharmacy&Technology etc. Recently few ion exchange resins (e.g. Indion 414) are found to have superdisintegrant property and are widely used in pharmaceutical industry. List of super disintegrants used for the formulation of orally disintegrating tablets with their mechanism of action were given in Table 2.

**List of Superdisintegrants for the Formulation of Rapid Disintegrating Tablets.**

<b>Superdisintegrants</b>	<b>Example</b>	<b>Mechanism of action</b>	<b>Special Comment</b>
Croscarmellose Ac-Di-Sol Nymce Zymce ZSX Primellose Solutab	Cross linked cellulose	Swells 4-8 folds in <10 seconds Swelling and wicking both	Swells in two dimensions Direct compression or granulation Starch free
Crosspovidone Crosopovidone M Kollidon Polyplasdone	Crosslinked PVP	Swells very little and returns to original size after compression but act by capillary action	Water insoluble and spongy in nature so get porous tablets
Sodium Starch glycolate Explotab Primogel	Crosslinked starch	Swells 7-12 folds in <30 seconds	Swells in three dimension and high level serve as sustain release matrix
Alginic acid NF satialgine	Crosslinked alginic acid	Rapid swelling in aqueous medium or wicking action	Promote disintegration in both dry or wet granulation
Soy polysaccharides Emcosoy	Natural super disintegrant		Does not contain any starch or sugar. Used in nutritional products

## TECHNOLOGIES FOR THE PREPARATION OF RAPID DISINTEGRATING TABLETS's

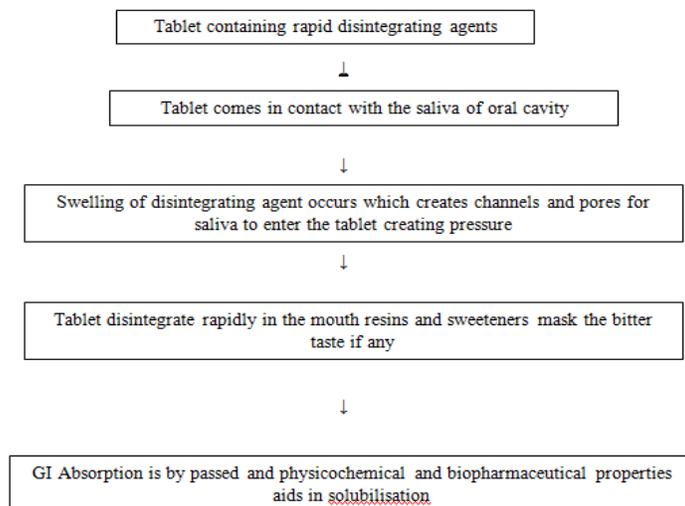
### 1) Conventional Techniques

- ❖ *Molding*
- ❖ *Freeze Drying*
- ❖ *Disintegrant addition*
- ❖ *Direct Compression*
- ❖ *Sublimation*
- ❖ *Mass extrusion*
- ❖ *Spray Drying*

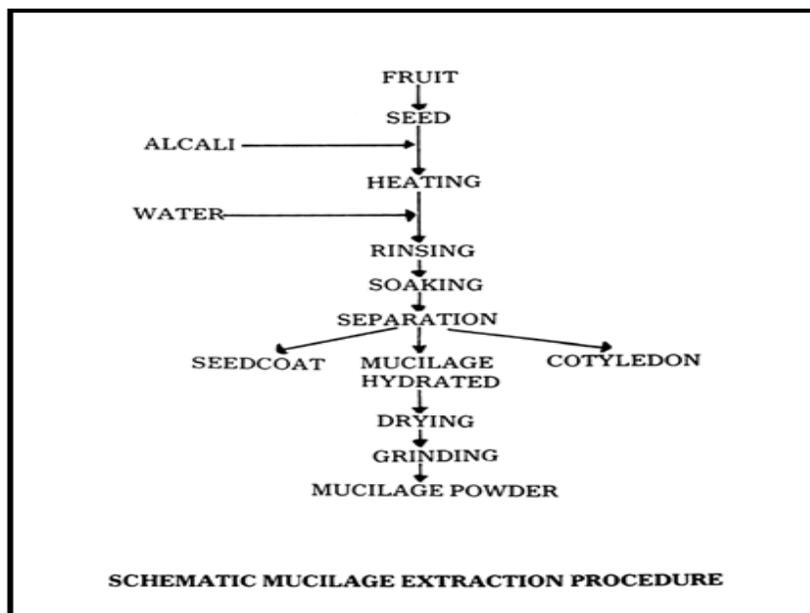
### 2) Patented technologies

- ❖ *Flash tab technology*
- ❖ *Orasolv technology*
- ❖ *Wowtab technology*
- ❖ *Flashdose technology*
- ❖ *Zydis technology*
- ❖ *Durasolv technology*

## Delivery Mechanism Of Rapid Disintegrating Tablet



## General Method Of Isolation Of Oscimum Basilicum Mucilage.



### Conclusion

The Rapid Disintegrating Tablets have potential advantages over conventional dosage forms, with their improved patient compliance; convenience, bioavailability and rapid onset of action had drawn the attention of many manufactures over a decade. The introduction of fast dissolving dosage forms has solved some of the problems encountered in administration of drugs to the pediatric and elderly patient, which constitutes a large proportion of the world's population. Hence, patient demand and the availability of various technologies have increased the market share of Fast dissolving tablets, which in turn prolongs the patent life of a drug. Keeping in view of the advantages of the delivery system, rapidly disintegrating dosage forms have been successfully commercialized, and because of increased patient demand, these dosage forms are expected to become more popular. Thus RAPID DISINTEGRATING TABLETS may be developed for most of the available drugs in near future.

Rapid Disintegrating Tablet is the selected drug delivery system as lamotrigine is used in the epileptic seizures thus it would be the best delivery system when one need a rapid onset of action.Choice of Lamotrigine which is BCS Class II drug, associated with its solubility problem thus onset of action is delayed which is not advisable for the patients with epileptic seizures. So by preparing a rapid disintegrating tablet of same would help in the formulation of such a dosage form which will overcome these mentioned disadvantages.Oscimum basilicum plant was procured from the local

nursery and the seeds were separated from same. A comparative study of number of synthetic superdisintegrants was done and the two superdisintegrants were selected based on the objective of the project and feasibility which are Cross linked alginic acid and cross linked PVP. Other excipients which are important for the formulation of rapid disintegrating tablet were selected. Isolation Of Oscimum Basilicum Seeds Mucilage From Oscimum Basilicum Seeds Was Performed Successfully. Isolated Oscimum Basilicum Seeds Mucilage Was Characterized On The Basis Of Its Organoleptic Properties, Micromeritic Properties ( Angle Of Repose, Bulk Density, Tapped Density, Compressibility Index, Hausners Ratio, Particle Size) Along With Melting Point And Solubility Determination Was Also Performed. Physicochemical Characterization Of Oscimum Basilicum Seeds Mucilage Is Also Done. All the test results are allowing to proceed further to use it as a superdisintegrant. Preformulation studies on Lamotrigine were performed including identification of drug by organoleptic properties study,  $\lambda$  max determination, FTIR studies and other parameters including Melting Point Determination , pH Determination, Partition Coefficient Determination, Solubility studies (Quantitative and Qualitative), Standard Curve in different solvent. It would be possible to get the rapid onset of action of the anti epileptic drug Lamotrigine and thus can control the serious epileptic convulsions in the minimum time.

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