



ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating: 5.03
TPI 2018; 7(5): 333-342
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www.thepharmajournal.com
Received: 25-03-2018
Accepted: 27-04-2018

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Comparative study on formulation and evaluation of fast dissolving Glibenclamide tablets: Opportunity in drug delivery system

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Abstract

Glibenclamide Tablets are used to lower blood sugar levels and are used in the treatment of late-onset diabetes (type II diabetes mellitus) in patients whose blood sugar is not controlled by diet alone and who are not suitable for insulin injections. The present work involves the formulation development, optimization and in-vitro evaluation of fast dissolving tablet containing Glibenclamide. All formulations were evaluated for characteristics such as hardness, friability, disintegration time and Dissolution rate. An effective, pleasant tasting formulation was found to have a good hardness of 3 kg/cm², disintegration time of 27+1 seconds and *in vitro* drug release of not less than 95% within 30 minutes. The drug release was found to be comparable with the marketed dispersible tablet. our drug meets all the criteria mentioned above. specially formulation 5 is best among all the formulations. The purpose of above study was to develop tablet of Glibenclamide using direct compression technique. The tablets were prepared using lactose and magnesium stearate with two different level of disintegrant. The super-disintegrant used in the study was starch. The total five formulations were evaluated for weight variation, thickness, hardness, friability, content of uniformity, disintegration time and dissolution characteristics

Keywords: Comparative study, formulation, evaluation, fast dissolving glibenclamide tablets, opportunity

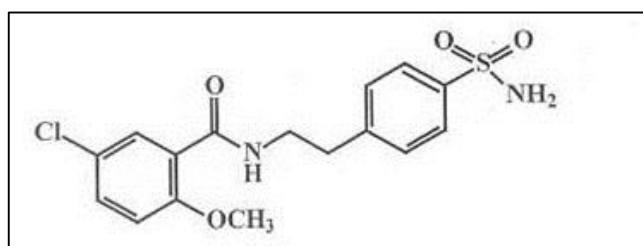
Introduction

A fast dissolving system can be defined as a dosage form for oral administration, which when placed in mouth, rapidly dispersed or dissolved and can be swallowed in form of liquid. Recently fast dissolving formulation is popular as NDDS because they are easy to administer and lead to better patient compliance. Pediatric and geriatric patient have difficulty in swallowing the conventional dosage forms. Fast dissolving and fast dispersing drug delivery system may offer a solution to these problems. Many patients find it difficult to swallow tablets and hard gelatin capsules and thus do not comply with prescription, which results in high incidence of noncompliance and ineffective therapy.

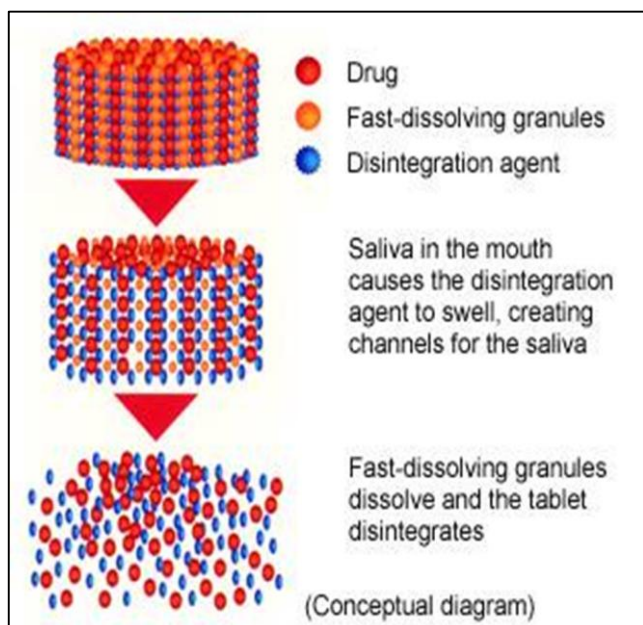
Fast disintegrating tablets are gaining prominence as new drug-delivery systems. These dosage forms dissolve or disintegrate in the oral cavity within a minute without the need of water or chewing. United States Food and drug administration (FDA) defined fast dissolving tablet (FDT) as “a solid dosage form containing medicinal substance or active ingredient which disintegrate rapidly usually within a matter of seconds when placed upon the tongue.” Fast dissolving tablets are also known as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapimelts, porous tablets, quick dissolving tablet. Fast dissolving tablets dissolve or disintegrate in the oral cavity without the need of water. Most fast dissolving tablets must include substances to mask the bitter taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients. It has been concluded that faster the dissolution, faster the absorption (only the unionized form of drug) and onset of action. Some drugs are absorbed from the oral cavity, pharynx and esophagus as the saliva passes down into the stomach. Thus the bioavailability of drug is significantly more than those observed from conventional tablets dosage form. The time for disintegration of fast disintegrating tablets [3] is generally considered to be less than one minute. The fast dissolving solid dosage form turns into a soft paste or liquid form for easy swallowing, and thus it is free of risk of choking. In recent years, a variety of improved methods for delivering drugs have been developed with the aim of improving bioavailability,

convenience and patient compliance. Some tablets are designed to dissolve in saliva within a few seconds, and so called true fast-dissolving tablets [4]. Glibenclamide (AAN, BAN, INN), also known as glyburide (USAN), is an antidiabetic drug in a class of medications known as sulfonylureas, closely related to sulfa drugs. It was developed in 1966 in a cooperative study between Boehringer Mannheim (now part of Roche) and Hoechst (now part of Sanofi-Aventis). It is sold in doses of 1.25, 2.5, and 5 mg, under the trade names Diabeta, Glynase, and Micronase in the United States and Daonil, Semi-Daonil, and Euglucon in the United Kingdom, and Delmide, Glybovin in India. It is also sold in combination with metformin under the trade names Glucovance, Benimet, and Glibomet, as well as Glucored and Glucored Forte (by Sun Pharmaceutical) in Russia, Belarus and other countries of the CIS.

Structure



Material



Salient features of FDTs

- Does not require water for oral administration
- Have sufficient strength to withstand the rigors of the manufacturing process and post manufacturing handling [5].
- Allow high drug loading.
- Insensitive to environmental conditions such as humidity and temperature.
- Adaptable and amenable to existing processing and packaging machineries.
- Cost effective.
- Have a pleasant mouth feel.

- Have an acceptable taste masking property.
- Be optimum harder and less friable.

Advantages

- Ease of administration to patients who refuse to swallow a tablet, such as pediatric and geriatric patients and psychiatric patients.
- No need of water to swallow the dosage form.
- Rapid dissolution and absorption of drug[6]
- Convenience of administration and accurate dosing as compared to liquids.
- Good mouth feel property helps to change the basic view of medication as "bitter pill", particularly for pediatric patients.
- Improved stability
- Suitable for controlled as well as fast release Actives
- Allows high drug loading.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Adaptable and amenable to existing processing and packaging machinery
- Cost- effective

Disadvantages [7]

- The tablets usually have insufficient mechanical strength. Hence, careful handling is required during manufacturing process.
- The tablets may leave unpleasant taste and/or grittiness in oral cavity if not formulated properly.
- Drugs with larger doses are difficult to formulate into FDT e.g. rifampin (600 mg), ethambutol (1000mg) etc.

Effectiveness factor

Dispersion in saliva in oral cavity causes pre-gastric absorption of drug which dissolves. Buccal, pharyngeal and gastric regions are all areas of absorption for many drugs [8]. Any pre-gastric absorption avoids first pass hepatic metabolism which increase the bioavailability. Furthermore, safety profiles may be improved for drugs that produce significant amounts of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism and for drugs that have a substantial fraction of absorption in the oral cavity and pre-gastric segments of GIT.

Manufacturing and marketing factors

As a drug nears the end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form. A new dosage form allows a manufacturer to extend market exclusivity, unique product differentiation, value-added product line extension, and extend patent protection, while offering its patient population a more convenient dosage form [9]. This leads to increased revenue, while also targeting underserved and under-treated patient populations. As examples, Eisai Inc. launched Aricept FDT, a line extension of donepezil for Alzheimer's disease, in Japan in 2004 and in the U.S. in 2005 in response to a generic challenge filed in the U.S. by Ranbaxy. Merck's Japanese subsidiary launched Lipola M (simvastatin ODT), a line extension of its block-buster, Zocor®, a cholesterol-lowering drug, in response to seventeen generic registrations of simvastatin applied for in Japan in 2004. Marketers build a better brand and in this way company's reputation can be improved.

Characteristics of fast disintegrating systems

FDDTs, as a novel dosage form, have several characteristics to distinguish them from the more traditional dosage forms. Traditional tablet formulations generally do not require taste masking, because it is assumed that the dosage form will not dissolve until passing the oral cavity. Many oral suspensions, syrups, and chewable tablets simply contain flavors, sugars and other sweeteners to overcome the bitter taste of the drug. In fast dissolving/disintegrating tablets include sweeteners and flavors for taste-masking but many bitter drugs are not masked by taste masking agent. The primary methods of taste-masking include adsorption onto or complexation with carriers and spray coating of drug particles.

Preparation methods of fast dissolving tablets

- Freeze drying
- Molding
- Sublimation
- Spray Drying
- Direct Compression
- Melt granulation
- Phase transition process ETC.

Freeze drying

A process, in which water is sublimated from the product after freezing, is called freeze drying. Freeze-dried forms offer more rapid dissolution than other available solid products. The lyophilization process imparts glossy amorphous structure to the bulking agent and sometimes to the drug, thereby enhancing the dissolution characteristics of the formulation.

The influence of various formulation and process parameters on the characteristics of rapidly disintegrating tablets in freeze dried form was investigated by Corveleyn and Remon who concluded that maltodextrins are useful in the formulation of fast dissolving tablets made by freeze drying.

The major disadvantages of lyophilization technique are that it is expensive and time consuming; fragility makes conventional packaging unsuitable for these products and poor stability under stressed conditions.

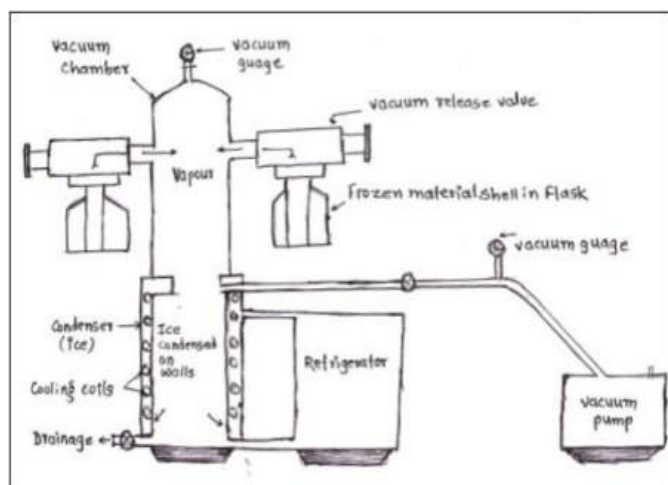


Fig 2: Freeze dryer

Molding

Tablet produced by moulding are solid dispersion. Moulded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is in general made from water soluble sugars. The active ingredients in most cases are

absorbed through the mucosal lining of the mouth.

The manufacturing process of molding tablets involves moistening the powder blend with a hydroalcoholic solvent followed by pressing into mold plates to form a wetted mass (compressing molding). The solvent is then removed by air drying. Thus the process is similar to what is used in the manufacture of tablet triturates. Such tablets are less compact than compressed tablets and possess a porous structure that hastens dissolution.

Sublimation

Because of low porosity, compressed tablets composed of highly water-soluble excipients as tablet matrix material often do not dissolve rapidly in the water. Porous tablets that exhibit good mechanical strength and dissolve quickly have been developed by Heinnemann & Rose, *et al.* Inert solid ingredients (ex. urea, urethane, ammonium carbonate, camphor, naphthalene) were added to other tablet excipients and the blend was compressed into tablet. Removal of volatile material by sublimation generated a porous structure.

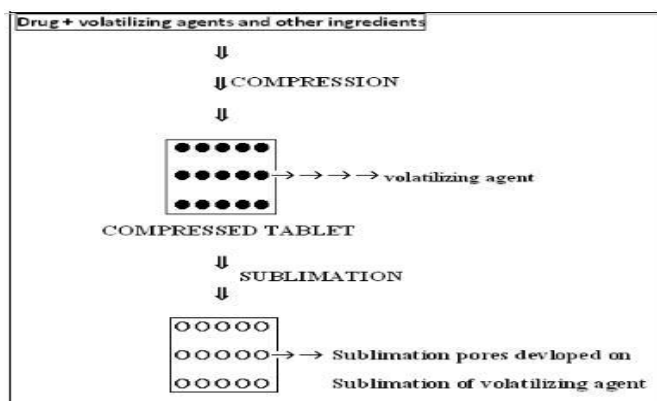


Fig 1: Schematic Diagram of Sublimation Technique for Preparation of FDT

Spray Drying

Spray dryers are widely used in pharmaceuticals and biochemical processes. Due to processing solvent is evaporated rapidly; spray drying can produce highly porous, fine powder. Spray drying can be used to prepare rapidly disintegrating tablets. This technique is based on a particulate support matrix, which is prepared by spray drying an aqueous composition containing support matrix and other components to form a highly porous and fine powder. This is then mixed with active ingredients and compressed into tablets.

Allen *et al* used a spray drying technique to prepare fast dissolving tablets. The tablets made from this technology are claimed to disintegrate within 20 seconds.

Direct Compression

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods [10]. Directly compressed tablet's disintegration and solubilization depends on single or combined action of disintegrates, water soluble excipients and effervescent agent. Disintegrate efficacy is strongly affected by tablet size and hardness. Large and hard tablets have disintegration time more than that usually required. As consequences, products with optimal disintegration properties often have medium to

small size and /or high friability and low hardness. Breakage of tablet edges during handling and tablet rupture during the opening of blister alveolus, all result from insufficient physical resistance.

Melt granulation

Melt granulation technique is a process by which pharmaceutical powders are efficiently agglomerated by a meltable binder. The advantage of this technique compared to a conventional granulation is that no water or organic solvents is needed. Because there is no drying step, the process is less time consuming and uses less energy than wet granulation. It is a useful technique to enhance the dissolution rate of poorly water-soluble drugs, such as griseofulvin. This approach to prepare FDT with sufficient mechanical integrity, involves the use of a hydrophilic waxy binder (Superpolystate, PEG-6-stearate). Superpolystate is a waxy material with a melting point of 33-37°C and a HLB value of 9. So it will not only act as a binder and increase the physical resistance of tablets but will also help the disintegration of the tablets as it melts in the mouth and solubilises rapidly leaving no residues [11].

Phase transition process [12]

It is concluded that a combination of low and high melting point sugar alcohols, as well as a phase transition in the manufacturing process, are important for making FDTs without any special apparatus. FDT were produced by compressing powder containing erythritol (melting point: 122°C) and xylitol (melting point: 93-95°C), and then heating

at about 93°C for 15 min. After heating, the median pore size of the tablets was increased and tablet hardness was also increased. The increase of tablet hardness with heating and storage did not depend on the crystal state of the lower melting point sugar alcohol.

Tablet Disintegrants

Bioavailability of a drug depends in absorption of the drug, which is affected by solubility of the drug in gastrointestinal fluid and permeability of the drug across gastrointestinal membrane. The drugs solubility mainly depends on physical - chemical characteristics of the drug. However, the rate of drug dissolution is greatly influenced by disintegration of the tablet.

The drug will dissolve at a slower rate from a nondisintegrating tablet due to exposure of limited surface area to the fluid. The disintegration test is an official test and hence a batch of tablet must meet the stated requirements of disintegration.

Disintegrants, an important excipient of the tablet formulation, are always added to tablet to induce breakup of tablet when it comes in contact with aqueous fluid and this process of desegregation of constituent particles before the drug dissolution occurs, is known as disintegration process and excipients which induce this process are known as disintegrants.

The objectives behind addition of disintegrants are to increase surface area of the tablet fragments and to overcome cohesive forces that keep particles together in a tablet.

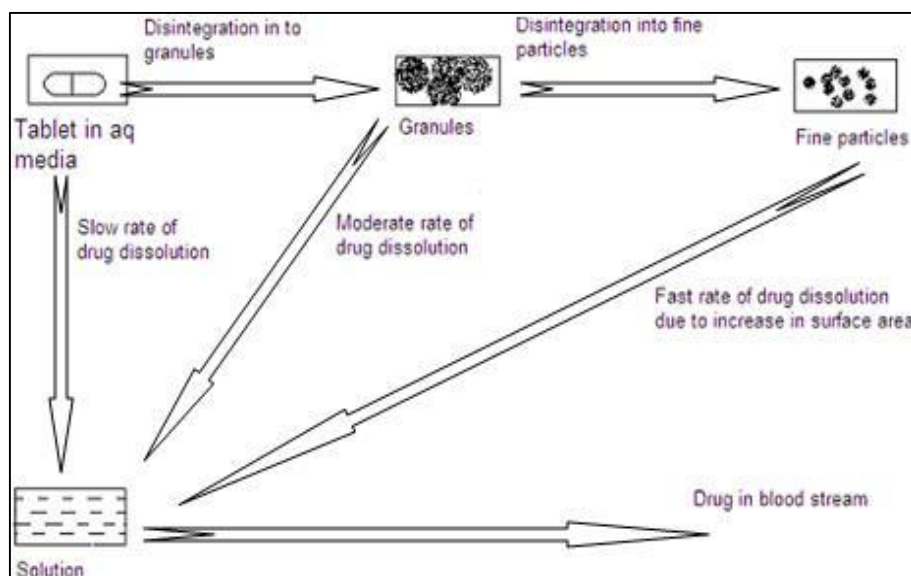


Fig 3: Schematic Representation Of Tablet Disintegration And Subsequent Drug Dissolution

Mechanism of tablet disintegration

- Capillary action (Wicking).
- Swelling.
- Due to disintegrating particle/particle repulsive forces.
- Due to deformation.
- Due to release of gases.

By capillary action

Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular

bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug /excipient and on tableting conditions. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

By Swelling

Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling. Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is

exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.

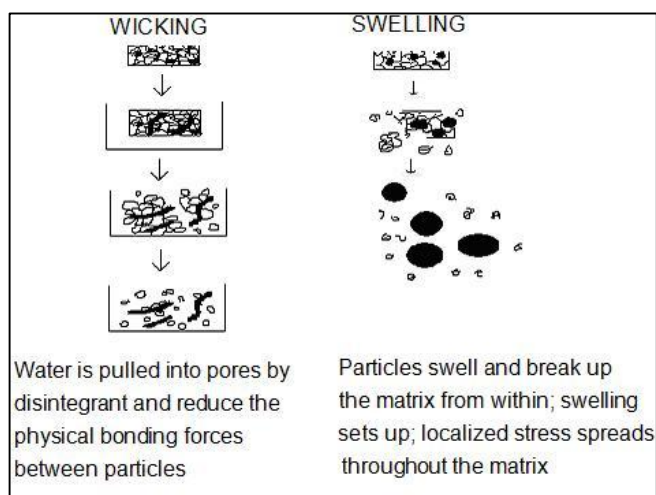


Fig 4: Disintegration of Tablet by Wicking And Swelling

Due to disintegrating particle/particle repulsive forces

Another mechanism of disintegration attempts to explain the swelling of tablet made with 'non-swelling' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. the electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.

Due to deformation

Hess had proved that during tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet. This may be a mechanism of starch and has only recently begun to be studied

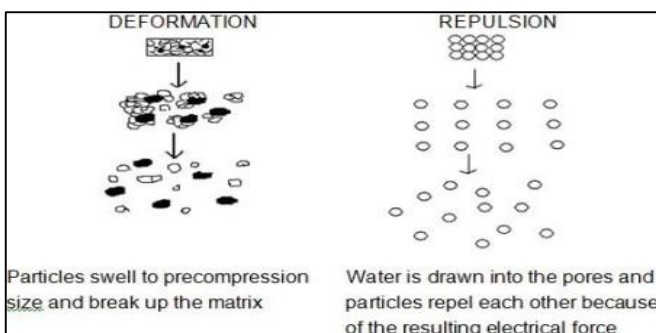


Fig 5: Disintegration by Deformation And Repulsion

Due to release of gases

Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. The tablet disintegrates due to generation of pressure within the tablet. This effervescent mixture is used

when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablet. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during manufacturing of the tablets. The effervescent blend is either added immediately prior to compression or can be added in to two separate fraction of formulation

Challenges in formulating FDTs

Palatability

Most orally disintegrating drug delivery systems disintegrate or dissolve in patient’s oral cavity, thus releasing the active ingredients which come in contact with the taste buds; hence, taste-masking of the drugs becomes critical to patient compliance.

Mechanical strength

In order to allow FDTs to disintegrate in the mouth, they are made with very low compression force, which makes the tablets friable and/or brittle, difficult to handle, and often requiring specialized peel-off blister packing that may increase the cost. Only few technologies such as Wowtab by Yamanouchi Shaklee and Durasolv by CIMA labs can produce tablets that are sufficiently hard and durable to allow them to be packaged in multidose bottles.

Hygroscopicity

Several FDTs 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. Amount of drug: For lyophilized dosage forms, the drug dose must be lower than 400 mg for insoluble drugs and less than 60 mg for soluble drugs.

Aqueous solubility

Water-soluble drugs 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.

Size of tablet: It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve.

Material and Methods

Glibenclamide was a gift from Amico Laboratories Ltd, starch, Lactose, Magnesium stearate, Crospovidon, Povidon-k30 and Talc were also collected from Amico Laboratories Ltd Khagan, Savar, Dhaka.

Ingredient details

S. No	Ingredient	Source
1	Kollidon CL	BASF South Est Asia Pte Ltd.
2	Lactose	DFE Pharma,Newzealand.
3	Avicel	Mingtai.Taiwan.
4	starch	Roquette Lestrem France
5	Talc	Asian Mineral Resoura corporation ltd,Thailand
6	Magnesium stearate	Nitika Pharma,India.
7	Povidon-K-30	Boai NKy pharma Ltd.

Instruments Details

S. No	Machine	source
1	Digital Weighing Machine	Nagata Fath Series, Taiwan.
2	Tablet Compression Machine	20 Menestry Tablet Compression Machine, England.
3	Monsanto Hardness Tester	Rolex Tablet Hardness Tester.
4	Friability Tester	Electrolab EF-2.USP.
5	USP Dissolution Apparatus	DBK Dissolution Rate Test Apparatus USP XXI.
6	Disintegration Apparatus	Electrolab ED-2 SAPO.
7	UV-Vis Doublebeam Spectrophotometer	1800 Shimadzu, Japan.

Method

Direct Compression

This method involves simple blending of active pharmaceutical ingredient (API) with other ingredients and direct compaction of the resultant mixture.

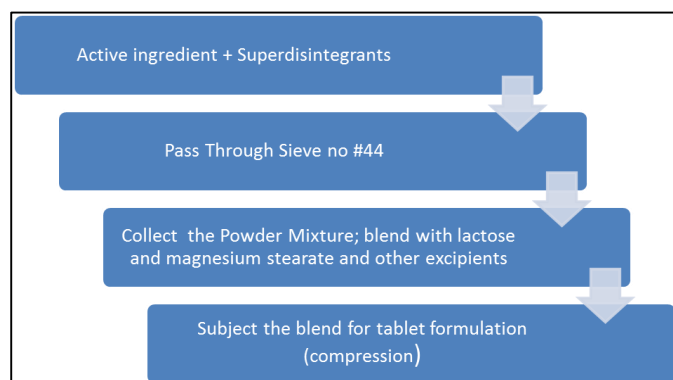


Fig 6: Schematic diagram of direct compression technique for design of fast dissolving tablets

Advantages of Direct compression

- **Cost Effectiveness:** The prime advantage of direct compression over wet granulation is economic since the direct compression requires fewer unit operations. This means less equipment, lower power consumption, less space, less time and less labor leading to reduced production cost of tablets.
- **Stability:** Direct compression is more suitable for moisture and heat sensitive APIs, since it eliminates wetting and drying steps and increases the stability of active ingredients. Changes in Dissolution profiles are less likely to occur in tablets made by direct compression on storage than in those made from granulations.
- **Faster Dissolution:** Disintegration or dissolution is the rate limiting step in absorption in case of tablets with poorly soluble API prepared by wet granulation. The tablets prepared by direct compression disintegrate into API particles instead of granules that directly come into contact with dissolution fluid and exhibits comparatively faster dissolution [13].
- **Less wear & tear of punches:** The high compaction pressure involved in the production of tablets by slugging or roller compaction can be avoided by adopting direct compression. The chances of wear and tear of punches and dies are less.
- **Other advantages:** As ingredients are processed for a shorter period of time, the chance for contamination is low. Due to fewer unit operations, the validation and documentation requirements are reduced and will become easier. Due to the absence of water in granulation, chance of microbial growth is minimal in case of tablets prepared by direct compression [14].

Limitations of Direct compression

- **Segregation:** Direct compression is more prone to segregation due to the difference in density of the API and excipients. The dry state of the materials during mixing may induce static charges and lead to segregation. This may lead to the problems like weight variation and content nonuniformity.
- **Cost:** Directly compressible excipients are the speciality products produced by spray drying, fluid bed drying, roller drying or co-crystallization. Hence, the products are relatively costly than the respective raw materials.
- **Low dilution potential:** Most of the directly compressible materials can accommodate only 30-40 % of the poorly compressible active ingredients like acetaminophen that means the weight of the final tablet to deliver the 500 mg of acetaminophen would be more than 1300 mg. The large tablets may create difficulty in swallowing.
- **Lubricant sensitivity:** Lubricants have more adverse effect on the filler, which exhibit almost no fracture or shear on compression (e.g. starch 1500). The softening effects as well as the hydrophobic effect of alkaline stearates can be controlled by optimizing the length of blending time to as little as 2-5 min.
- **Variation in functionality:** There is a lack of awareness in some situations that the excipient behave differently, depending upon the manufacturer so much so that substitution from one source to that of another is not possible. Hence, there is a need for greater quality control in purchasing of raw materials to assure batch uniformity.

Factors influencing the selection of optimum DC vehicle

- Properties of Powders. (particle size, shape, density, solubility)
- Properties of compacts. (flow, compatibility)
- Stability factors. (temperature and moisture effects)
- Others. (Cost, availability etc.)

Formulation of Glibenclamide fast dissolving tablets

All the materials were passed through 80 # screens prior to mixing. Glibenclamide, Avicel PH 102, Starch, were mixed using a glass mortar and pestle. All the materials were directly compressible so this uniformly mixed blend was compressed into tablets using concave face round tooling on a Rimetrotary tablet machine. In the present research work mouth dissolving tablets of Glibenclamide was developed with superdisintegrant like starch in various concentration like 4%,5%,6%,7% & 8% w/w by direct compression method. All formulations were evaluated for physical characteristics of compressed tablets such as weight variation, hardness, friability, content uniformity, *in vitro* disintegration time and *in vitro* dissolution study.

Table 1: Different Formulation of Glibenclamide Fast dissolving tablet

Ingredient	Batch 1	Batch 2	Batch 3	Batch 4	Batch 5
Glibenclamide	5.25	5.25	5.25	5.25	5.25
Avicel PH 102	20	20	20	20	20
Lactose	118	116	114	112	110
Crospovidon	8	10	12	14	16
Magnesium Stearate	4	4	4	4	4
Talc	2	2	2	2	2
Povidon K30	3	3	3	3	3
Starch	4	4	4	4	4
Total	164.25mg	164.25mg	164.25mg	164.25mg	164.25mg

Total observation of formulations during these process are shown in a chart which was given by the expertise of the Amico Laboratories Ltd in respect to a marketed drug product.

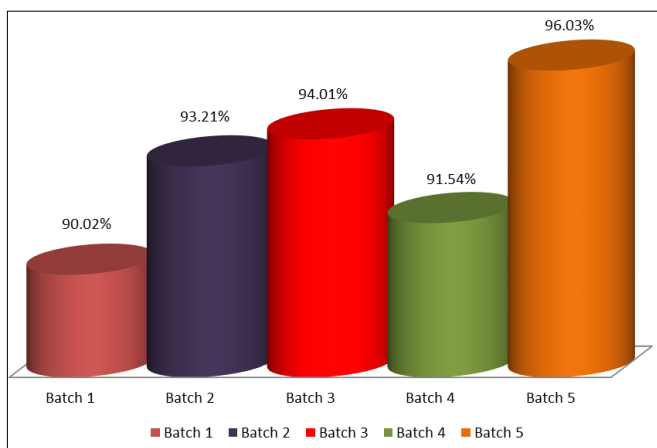


Fig: comparative evaluation of all the formulations

Evaluation of Glibenclamide fast dissolving tablets

For assessing weight variation ten tablets were selected at random and assessed individually using an Analytical balance (Adair Dutta, AD-50B, and Kolkata). The individual weights were compared with the average weight for determination of weight variation; Hardness [14] and friability of the tablets were determined by using a Monsanto hardness tester and a Roche friabilator, respectively. For content uniformity test, 20 tablets were weighed [16] and powdered, a quantity of powder (200 mg) was dissolved with 0.1N HCl and the solution was filtered through 0.45 μ membrane (Nunc, New Delhi, India). The absorbance was measured at 286 nm after suitable dilution. The *in vitro* disintegration test was carried out on six tablets using USP disintegration test apparatus with distilled water at 37±0.5° and the time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

General Appearance

The general appearance of a tablet, its identity and general elegance is essential for consumer acceptance, for control of low-to-lot uniformity and tablet-to-tablet uniformity [17]. The control of general appearance involves the measurement of size, shape [18], color, presence or absence of odor, taste etc.

Size & Shape

It can be dimensionally described & controlled. The thickness of a tablet is only variables. Tablet thickness can be measured by micrometer or by other device. Tablet thickness should be controlled within a ± 5% variation of standard value.

Weight variation

Variation between tablet with respect to dose and weight must be reduced to a minimum. Uniformity of weight is an in process test parameter which ensures consistency of dosage units during compression.

Test Procedure

Weigh individually 20 units selected at random and calculate the average weight. Not more than two of the individual weights deviates from the average weight by more than the percentage given in the pharmacopeia and none deviates by more than twice that percentage. IP/BP & USP limits for tablet weight variation is given below.

IP/BP	Limit	USP
80 mg or less	± 10%	130mg or less
More than 80mg or Less than 250mg	± 7.5%	130mg to 324mg
250mg or more	± 5%	More than 324mg

We know our tablets individual weight is 200mg.so, the prescribed limit for weight variation according to BP is ±7.5% that means 185∞215mg.

Batch 1	Batch 2	Batch 3	Batch 4	Batch 5
163.1mg	0.1633mg	0.160mg	0.161mg	0.163mg
0.159mg	0.162mg	0.157mg	0.164mg	0.167mg
0.163mg	0.163mg	0.167mg	0.176mg	0.158mg
0.181mg	0.165mg	0.163mg	0.164mg	0.169mg
0.171mg	0.166mg	0.178mg	0.167mg	0.161mg
0.162mg	0.162mg	0.167mg	0.179mg	0.173mg
0.166mg	0.167mg	0.158mg	0.164mg	0.174mg
0.162mg	0.166mg	0.165mg	0.160mg	0.172mg
0.165mg	0.163mg	0.165mg	0.161mg	0.173mg
0.163mg	0.165mg	0.164mg	0.181mg	0.166mg
164mg (avg)	164mg (avg)	164mg (avg)	164mg (avg)	164mg (avg)

All the batches is within our limit. So our weight variation test is perfect for all batches.

Thickness

The thickness of tablets is critical to their therapeutic effectiveness.

All tablets, where the active ingredient comprises a major part of the tablet are required to meet a weight variation test. It is assumed that providing the weight of the tablet is kept within defined limits that the amount of active drug available to the user will remain the same.

The weight of a compressed tablet is dependent on three factors:

density, diameter and thickness. In theory, the density of the powder blend and the diameter of the resultant tablet (which is dictated by the die wall) should remain unchanged[19].

It follows that by monitoring the thickness of the tablets at

regular intervals, potential problems relating to tablet weight and hence content uniformity can be detected at an early stage [20].

The calipers and thickness testers featured in this section are

Batch 1	Batch 2	Batch 3	Batch 4	Batch 5
3.75	3.75	3.75	3.75	3.75
3.75	3.75	3.75	3.75	3.55
3.75	3.75	3.75	3.75	3.78
3.75	3.75	3.55	3.75	3.71
3.75	3.75	3.78	3.75	3.75
3.75mm (avg)	3.75mm (avg)	3.71mm (avg)	3.75mm (avg)	3.71mm (avg)

Hardness

Tablet hardness has been defined as the force required breaking a tablet in a diametric compression test. To perform this test, there is a Tablet Hardness tester (Monsanto tester). The tablet is placed between two anvils, force is applied to the anvils and the crushing strength [21] that just causes the tablet to break is recorded. Hardness is thus sometimes termed as the tablet crushing strength.

Batch	Hardness (kg/cm ²)
1	3
2	3
3	3
4	3
5	3

Friability

The friability of tablets is determined by friability apparatus (.). 20 tablets were taken and weighed. After weighing the tablets were placed in the friabilator and subjected to the combined effects of abrasion [23] and shock by utilizing a plastic chamber that revolves at 25 rpm for 4 minutes dropping the tablets from a distance of six inches with each revolution. After operation the tablets were de-dusted and reweighed. Friability is determined by

$$F = \frac{(1st\ weight - 2nd\ weight)}{1st\ weight} \times 100$$

Batch	F = $\frac{(1st\ weight - 2nd\ weight)}{1st\ weight} \times 100$	Result
1	$\frac{3.27 - 3.26}{3.27} \times 100$	0.30%
2	$\frac{3.49 - 3.47}{3.49} \times 100$	0.57 %
3	$\frac{3.36 - 3.34}{3.36} \times 100$	0.59%
4	$\frac{3.50 - 3.48}{3.48} \times 100$	0.57%
5	$\frac{3.36 - 3.34}{3.36} \times 100$	0.59%

The acceptable limits of weight loss should not be more than 1 percent. So, all the batches are within our limit.

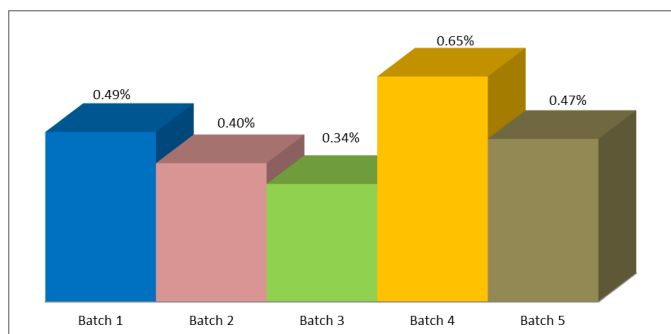


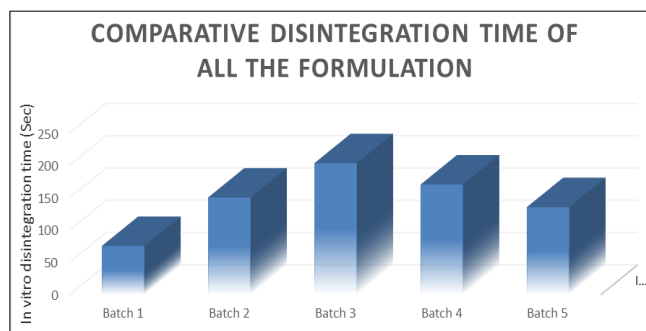
Fig: Comparative friability test of all the formulation

simple, easy to use instruments designed for use by the press operator on the compression floor. In this case we used a vernier caliper to detect tablets diameters.

In-vitro disintegration test

The test was carried out on 6 tablets using Tablet disintegration tester (Electrolab, India). Distilled water at 37°C ± 2°C was used as a disintegration media and the time in seconds taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

Batch	In vitro disintegration time (Sec)	Result
1	1	0∞1 min
2	49	0∞1 min
3	49	0∞1min
4	49	0∞1 min
5	49	0∞1 min



Content uniformity test

Assay (By UV Spectrophotometer)

The Fast dissolving tablets were prepared and evaluated for assay. Each FDT contains 10mg of Glibenclamide

Preparation of standard solution

Accurately weigh and transfer about 10mg of Glibenclamide working standards into a 50ml volumetric flask. Add about 40ml 0.1M of HCl and sonicate to dissolve [24]. Dilute to volume with Diluents and mix. Transfer 10ml of the above solution into a 50ml volumetric flask, dilute to volume with 0.1M HCl and mix.

Preparation of sample solution

Transfer 10 tablets into a mortar and crushed into fine powder blend. Weigh 560mg equivalent sample from this and transfer into a 50 ml volumetric flask. Add about 40ml 0.1M of HCl and sonicate to dissolve. Dilute to volume with Diluent and mix and then filter the solution [25]. Transfer 10ml of the above solution into a 50ml volumetric flask, dilute to volume with 0.1M HCl and mix.

Procedure

Flush the UV Spectrophotometer cuvettes thoroughly with water followed by HCl. Stabilize the system for not less than

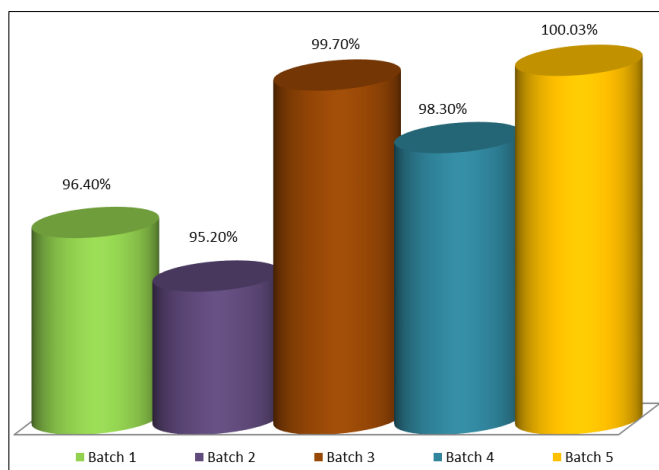
30minutes with blank solution (0.1 M HCl). Samples are typically placed in the cuvettes containing standard solution and blank as a reference in another cuvette, this is measured

$$\text{Glibenclamide} = \frac{\text{sample absorbance}}{\text{standard absorbance}} \times \frac{\text{standard weight}}{\text{sample weight}} \times \frac{\text{standard potency}}{100} \times \text{average tablet weight}$$

And as

$$\text{Glibenclamide} = \frac{\text{Result}}{99.10\%}$$

Sample ID	Wave length	Glibenclamide	Glibenclamide
1	300	1.611g (average)	161mg/tab
2	300	1.633g (average)	163mg/tab
3	300	1.644g (average)	164mg/tab
4	300	1.633g (average)	163mg/tab
5	300	1.633g (average)	163mg/tab



Our tablet acceptable limit is 95% -105%.so our all formulations are within our limit and among them formulation 5 is best.

Result and Discussion

In the present study, Glibenclamide fast dissolving tablets were prepared by using, Microcrystalline Cellulose (Avicel pH-200), starch and as superdisintegrants. A total number of 5 formulations were prepared by direct compression. The value of pre-compression parameters evaluated were within prescribed limits and indicated good flow property.

The data obtained of post compression parameters such as hardness, friability, weight variation, uniformity of content, thickness, disintegration time are shown above. The hardness was found to be in range of 2 to 3 kg/cm² in all the formulations indicating good mechanical strength with an ability to withstand physical and mechanical stress conditions while handling. In all the formulations the friability value is less than 1% and meets the BP (British Pharmacopoeia) limits. All the tablets passed weight variation test as the % weight variation was within the pharmacopoeia limits. The weight of all the tablets was found to be uniform with low standard deviation values indicating efficient mixing of drug, superdisintegrants and excipients. The percentage drug content of all the tablets was found to be between (95 to 105) of Glibenclamide, all the formulations which was within the acceptable limits. Overall the Fast Dissolving Tablets of Glibenclamide showed an average of more than 90 % drug release range at the end of 45 min which is as per BP specifications of 90-110 % and it was also observed that formulations 5 took shortest time to release the maximum

amount of drug whereas the other formulations took more than 45 min to release the drug. Comparison with other formulations, 3 shows a better drug release of 95.09 % at the end of 45 minutes. Further the formulation 5 was compared with marketed formulation (XEPADON, AMICO LABORATORIES LIMITED) and found to be superior in terms of dissolution profile.

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Conclusion

Direct compression method can be considered as an important method for the formulation of fast dissolving tablets of Glibenclamide compare to wet and dry granulation method. The rank order for the best 3 formulations is B5> B3 > B4. Formulation B5 having starch as the superdisintegrant is the best formulation of all. Higher the concentration of the lubricating agent (Magnesium Stearate or Talc), higher will be the disintegration time. Formulation having the better superdisintegrant with higher concentration will have better *in vitro* disintegration time and dissolution along with lesser friability and weight variation. Thus, it may be concluded that the fast dissolving tablets of Glibenclamide can be successfully prepared and undoubtedly the availability of various technologies and manifold advantages of fast dissolving tablets will surely enhance patient compliance and its popularity in the near future.

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