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EMBRACING THE QUALITY IN ALTERNATIVE ORAL DRUG DELIVERY SYSTEM: ORAL DISINTEGRATING TABLET (ODT)

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ABSTRACT
By performing the present literature survey it is ensured that ODT plays a vital role towards the oral drug delivery systems to target the efficacy, safety and patient acceptability. Out of those, drug delivery system being very eminent among pediatrics and geriatrics is orally disintegrating tablet (ODT). These Oral disintegrating tablets have superiority as the latter are associated with the risks of choking and friability. This drug delivery system has numerous advantages over conventional tablets as they can be used for verities of diseases and are taken without water due to their ability to disintegrate within a few seconds releasing drug in mouth. Various approaches are employed for formulating ODTs. Generally; hydrophilic polymers along with other excipients are used for preparing ODTs which allow Tablet to disintegrate quickly releasing incorporated active pharmaceutical ingredient (API) within seconds. Orally disintegrating tablets have potential for business and market exploitation because of their myriad of benefits over orally disintegrating tablets. This present review attempts to focus on quality system in ODTs formation, approaches for formulation and evaluation of ODTs.

KEYWORDS: ODT (Oral Disintegrating Tablet), QbD (Quality by Design), Oral Drug Delivery System.

INTRODUCTION
Recent advances in the Novel Drug Administration System have been designed to prepare dosage forms, formulation, to eliminate convenient side effects, to offer immediate release and improve bioavailability hence the patient is better Compliance can happen. However, the oral medication administration system will be better. Tablets are an equally acceptable dosage form, which provides a uniform dose and painless delivery. It is approximately 45% of the normal population and is associated with several types of diseases such as inflammation, menstrual pain, migraine, analgesia, pyrexia, emesis, Parkinson's disease, etc.[1]

It is always the purpose of a designer or a scientist to formulate a dosage form & to increase the safety of user while to maintain its therapeutic efficacy and to develop such a distribution system, i.e., an oral disintegrating tablets (ODT). The pharmaceutical quality technologists have done everything possible.[2]

To overcome these problems, some new drug delivery systems have been developed, such as the oral disintegrating tablet (ODT). These novels are dosage forms that disintegrate in saliva at a specific time during tongue placement. This type of ODT can be administered anywhere and anytime without the need for water, making it very suitable for children, the elderly, the disabled and patients with mental disabilities. The oral drug delivery system is becoming increasingly sophisticated as pharmaceutical scientists gain a better understanding of the physical and biochemical parameters for their performance. Despite the tremendous progress in the administration of medications, due to the low cost of medical care, the easy administration of the dose, self-medication, pain prevention, versatility, the high level of patients taking the oral route, the correct way to administer medical agents Compliance has passed.[3]

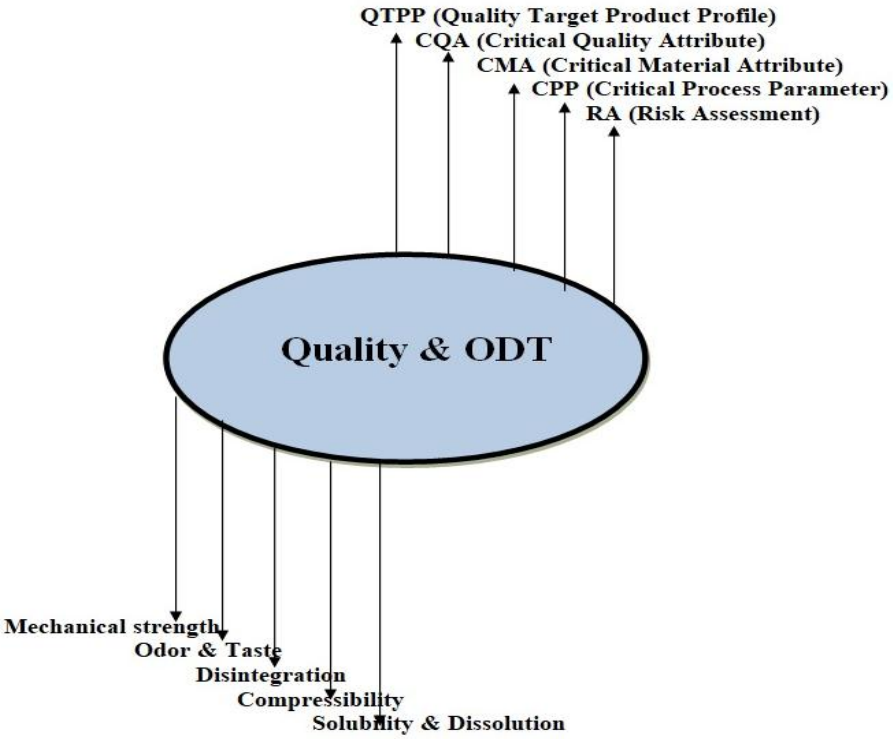
The US FDA has defined the ODT as "A solid dosage in which there is a medical substance or an active ingredient that discharge rapidly, usually within a few seconds of being placed on the tongue"; Dissolution is limited from seconds to minutes. In addition to concerns about rapid disruption, extraneous formulations must also provide an adequate taste mask, since the pill disintegrates in the oral cavity, so that the medication can come into direct contact with the patient's taste buds.[4]

Some excipients have versatility and the process is being initiated, while the selection of these excipients and also the process also depends entirely on the quality approach to prepare a product of spatial quality designed systematically. The design and development of the oral disintegrating tablet (ODT) is one of the largest

sequences to produce the product. The role of QbD in ODT is to expand creative planning, risk assessment and regulatory approval. The large-scale process in QbD involves the transformation of small-scale development and distribution.[5]

Elements of Quality System

The aspect of QbD is composed of following elements that follows to the entire development of Oral Disintegrating Tablet (ODT).[6]



1) QTPP (Quality Targeted Product Profile): Quality objective product profile creates design basis for product development. Ideas for the quality profiles may include: Route of administration, dosage form, dosage power, disintegration, aerodynamic performance.[7]

2) CQA (Critical Quality Attributes): CQA is a property or physical, chemical, biological or microbiological property that must be within a reasonable range, or distribution to guarantee the quality of the desired product. The CQAs are generally associated with pharmacological substances, excipients, intermediate products and pharmaceutical products. The CQAs of solid oral dosage forms are generally the aspects that affect purity, potency and drug release and product stability. For other distribution systems, the CQAs may include additional product-specific aspects, such as thermodynamic properties for breath products, parenteral sterility, and adhesion properties for transdermal patches. For pharmacological substances, raw materials and intermediates, CQAs may additionally include those properties (e.g., particle size distribution, bulk density) that affect the CQAs of pharmaceutical products.[8]

3) CMA (Critical Material Attributes): A property or physical, chemical, biological or microbiological property of the input material that must be within a reasonable range, range or distribution to guarantee the desired quality of the output material.[9]

4) CPP (Critical Process Parameters): A potential summary of the quality characteristics of a drug molecule is ideally obtained to ensure the desired quality, taking into account the safety and efficacy of the pharmaceutical product.[10]

5) RA (Risk Assessment): The risk assessment is usually carried out quickly in the dosage form development process and is repeated because more information is available and obtained. Based on prior concepts and initial experimental data, risk assessment tools can be used to identify and classify the parameters that are likely to affect the quality of the product (for example, process, equipment, input content). The initial list of potential parameters can be quite broad, but additional studies can be modified and prioritized (for example, experiments, through the combination of the design of the machine model). The list can be further refined by using the experiment to determine the importance of individual variables and possible interactions. Once the important parameters have been identified, they can obtain a greater level of understanding of the process, through the design of experiments, mathematical models or studies that lead to mechanical understanding can be studied.[11]

Advantages of Quality System

- ✓ It ensures that the drug delivery is efficient, potent and fit to administer.
- ✓ This approach eliminates to the failure chances of the entire formulation by risk analysis.
- ✓ It provides the flexibility in to formulation designing system.
- ✓ Correlations of multiple variables rather than outputs of single variables
- ✓ Specification criteria based on curve fitting factors rather than single output limits.
- ✓ The elimination of some end product testing for product release.
- ✓ Arrival at a very thorough manufacturing process understanding.

Eliments Assesments in ODT

Critical Quality Attributes (CQAs) for ODT

Quality Attributes	Target	Rational
Mechanical Strength	Less friable/brittle	ODTs should have a porous matrices or be compressed with very low compression force, soft, friable. In other hand, tablets with high mechanical strength leads to a larger disintegrating time. to get the quality product.
Taste and odour	Sweet/sore	Excipients used in the formulation or super disintegrate are basically tasteless while must not passage malodour that influence the patient acceptance.
Disintegration	Within the mouth cavity	Due to aqueous environment within the oral cavity the excipients being used in the formulation must hydrophilic and water soluble. Thus directly impact on the quality of product.
Dissolution	Sparingly Soluble/Slightly soluble	In addition, pre-formulation studies demonstrated that polymorph does not undergo any polymorphic conversion under the various stress conditions tested. Thus, the polymorphic form must be further evaluated on drug product specifications.

Quality Target Product Profile (QTPP) for ODT

Qtpp Element	Target		Rational
Dosage form	Oral Disintegrating Tablet (ODT)		Embracing Patient Compliance.
Rout of Administration	Oral		Drug Passage absorption in gastric region.
Shape of Dosage form	Spherical to Round		Easy to patient intake.
Drug Product Targeted Attributes	**Disintegration time**	5-30 sec in 6.8 buffer	All these attributes ensure to the patient acceptability while does not directly impact to the drug performance.
	Appearance	Better acceptance by the patient.	
	Odor & Taste	Better acceptance by the patient	
	Drug Release	90-95%	All of these attributes will directly impact to the safety and efficacy of the drug.
	Content Uniformity	90 –110%	

Critical Material Attributes

S NO	Material Attributes	Specification	Rational Justification
1	Identification	Chemical Identified	Leads to the undesirable effect.
2	Assay	90-110%	Failure to comply may cause fewer efficacies.
3	Colour	White/yellowish/Off white	Fails to identification.
4	Moisture Content	5-10%	Hydrolysis may entrap.
5	Impurity	Less than 2 ppm	Leads to the complexation
6	pH	5-8	Beyond the Limit can decomposition of formulation
7	Microbial Content	Negative	Decomposition of Entire product

ODTs for Varieties of Therapeutic Categories

S NO.	Therapeutic Agent	Pharmacological Class	Conclusion of Innovation	Year of Development (Author Name)
1	Mosapride Citrate	Selective 5HT3 Agonist	Vomiting centre is a highly sensitive area as s site of action for serotonin receptor agonist thus the patient required immediate onset of action which allows patient for rapid effect.	2018 W.Tong
2	Nimodipine	Antihypertensive	Anti hypertension induced due to aldosteron release where calcium channel blocker like Nimodipine is most suitable to formulate as ODT.	2017 S.D Shahwaj
3	Ibuprofen	NSAID	Pain and inflammation plays as an integrated role of a indicator that indicate to the abnormality inside the body where for enhancing the patient convenient ODT for Ibuprofen has been formulated.	2016 V.Ashwani
4	Quetiapine Fumarate	Antipsychotic	Psychosis is one if the neurological disease caused by malfunctioning of neurotransmitter thus for betterment of therapeutic efficacy ODT is an effective approach.	2015 P. Kalyankar
5	Desloratadine	Antihistaminic	Gastric oesophagus refluxes is one of the common class of disorder which undergo immediate onset of action desloratidne oral disintegrating tablet may resolved.	2014 A.Mohamed
6	Pentoprazole Sodium	Antiulcer	Ulcer is a mucodegradation caused by various conditions where proton pump is one of the major causes in order to overcome such issue ODT for pentoprazole has introduced.	2013 M. Jaimin
7	Nimesulide	NSAID	Prostaglandin is auto releasers produced by cyclooxigenase pathway while Nimesulide is NSAID class that prevent the synthesis of such pathway.	2012 A. Thulluru
8	Cinnarizine	Antihistaminic	Asthma is class of disease that also known as COPD thus delivery of antihistaminic drug like cinnarizine as ODT cure such problem.	2011 G.Prajapati

Quality Assessment of Attributes

a) Pre Compressions Assessment

i) Bulk Density: It is referred to the pre compression attribute that stands for the total mass of test substance fractionally equal to its bulk volume.[12]

$$\text{Bulk Density} = \frac{\text{Mass of substance}}{\text{Bulk volume}}$$

ii) Tapped Density: It is referred to the pre compression attribute that stands for the total mass of test substance fractionally equal to its Tapped volume.[13]

$$\text{Tapped Density} = \frac{\text{Mass of substance}}{\text{Tapped volume}}$$

iii) Compressibility index: It is the propensity of a powder to be compressed. Based on the apparent bulk density and Tapped density the percentage compressibility of the blend is determined using the following formula.[14]

$$\text{Compressibility index} = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \times 100$$

iv) Hauser's ratio: It indicates the flow properties of the powder. The ratio of Tapped density to the bulk density of the powders is called Hauser's ratio.[15]

$$\text{Hauser's ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

v) Angle of repose: The Angle of repose may determined by passing the bulk mass through a funnel fixed to a burette stand at a particular height (4 cm). The height and radius of the pile is measured. Angle of repose of the blend is calculated using the formula: Where, h = Height of the pile r = Radius of the pile.[16]

Angle of repose = tan⁻ h/r

b) Post Compression Assessment

i) Water Absorption Ratio: Due to its presence inside the saliva, it is necessary to analyze the water absorption ratio for ODT. To perform this type of test, the tissue paper is removed with folds twice under the small amount of water inserted in the petridis while the tablet falls on the wet paper. The water absorption ratios can be calculated by measuring the wet tissue paper and the weight of the tablet.[17]

ii) Crushing Index: The oral disintegrating tablet is driven to crush the oral cavity; therefore, the monsanto-type hardness tester can determine the crush resistance of the tablet, while the tester is placed on the advantageous scrolling tip so that the tablet is crushed to record values. About 10 tablets are required to do this type of test.[18]

iii) Friability: Friability is the relationship between the removals of particles from the surface of the tablet, which is partly related to the weight loss between the total weights. Values are determined by taking 20 tablets to maintain for 4 minutes after 25 rpm. The friability should not be different with 1%.[19]

iv) Weight Variation Test: The weight variation test is essential to load a sufficient amount of uniform contents. It is also believed that this feature covers the quality of the ODT.20 tablets undergo such tests, while uniformity should be followed by the fraction between the initial weight and final weight of dosage form.[20]

v) In Vitro Disintegration Test: In vitro evolution may carried out by performing 900 ml of distilled water are made according to the pharmacopoeia at 37°C to 2°C. Six of tablets has been placed in each of the six tubes immersed in distilled water unit. A disc is added to each tube. The time required for the complete disintegrate of the tablet until no mass remains in the tube, is considered the disintegration time.[21]

vi) Dispersion Adoption: This test is carried out by placing 2 tablets in 100 ml of water and shakes it slowly until the tablets are fully extended. The formulation is thought to make a smooth dispersion if a nominal filter of 710 μ of trap passes without leaving the residue in the mesh.[22]

vii) Wait Time: Crepuscular paper is stored in the Petri dish, which has an internal diameter of 5 cm, which contains 6 ml of water. A tablet containing a small amount of rasaline powder on the top surface is placed on the tissue paper. The time needed to develop the red colour on the top surface of the paper is considered wet time.[23]

Application of Quality System in Oral Dosage form

Dosage Form	Specification		Risk Assessment
Tablet	Precompression	Weighing	Calibration process of weighing balance.
		Dry Mixing	Geometrical Rotation Speed of blender.
		Sieving & Shifting	Viberational Ratio of Sieve Shaker.
		Granulation	Speed of Impeller and Chopper in granulator.
		Drying	Temperature and Time Duration.
	Compression	Compression force	The tooling of compression machine leads to full fill the assessment.
		Fill Weight	
		Fill Volume	
		Punch Size	
Capsule	Shell process	Dipping	The dipping solution to simultaneously form the shell
		Spinning	Formation of a bead at the capsule ends.
		Drying	Rate of cool air to form hard shells.

Literature Review

Siddiqui N.M., *et.al.* (2018): It has been found in the study that the ODT concept has been developed to overcome some problems present in the conventional solid dosage i.e. the problem swallow in paediatric and geriatric patients, which is an important part of world population Due to the rapid absorption of GIT from the mouth ODT that enhance the efficacy, bioavailability, the onset of acute action better patient compliance. The outside body shot quickly dissolves and acts as a solid dosage ODT in the future may be as the most acceptable and prescribed dose due to its rapid action (in minutes) when administered.[24]

Gujarati N., *et.al.* (2017): It has been studied that seven out of ten medical professionals believe that a fast dissolving antidepressant tablet will improve compliance and 50% say that rapid dissolving antidepressant therapy is half useful, most or all your depressed patients. Other research shows that 5% of depressed patients prefer on the sun tab for a traditional tablet, and 43% say they are more likely to take medications in the form of pills that dissolve quickly.[25]

Ugurlu T., *et.al.* (2015): Introduced to oral disintegrating tablet has many benefits compared to other forms of oral dosage, such as better bioavailability, better patient compliance and better efficacy. However, limited challenges such as the limited weight of the tablet, interruption time, stability, manufacturing technology and packaging should be considered. Tablets for verbal interruption can be evaluated as the first choice for mental and geriatric medications, which cannot be used specifically for the central nervous system, gastrointestinal disorders and pain.[26]

Buket A., *et.al.* (2014): The drug model was examined, it was shown that the ANN approach can be used to ease and use with success, and this approach can be beneficial in terms of raw materials, time and cost.[27]

Sharma D., *et.al.*(2013): By saying that there is a promising approach with a tablet approach that quickly disintegrates to accelerate the drug performance and will be beneficial compared to the traditional dosage forms currently available. The dosage form has a good balance between dissolution time and mechanical strength. The main objective of the study was to develop the rapid disintegration tablet of cetirizine hydrochloride, generally using the available excipients and conventional technology. From the previous study, it was concluded that a rapidly dissolving tablet of cetirizine hydrochloride can be developed using medicinal excipients, such as super-disintegrates, hydrophilic and inflammatory excipients and an adequate charge, which can be commercial.[28]

Jain N., *et.al.* (2012): Ciprofloxacin oral disruptive pills with adequate mechanical strength, acceptable flavours and small interruption time at the optimal concentration of supersonic agents and other excipients were employed. The stability studies showed that there was no significant change in the dissolution of the drug content and the oral disintegrating tablet. The FTIR studies have shown that there were no changes in the peaks, shows that there is no dialogue between ciprofloxacin and other materials used. In the two super-disintegrates used like crosspovidone performed better at the time of dissolution compared to sodium starch glycolate.[29]

Mishra M., *et.al.* (2011): ODT formulation with the desired quality characteristics. With the results of the current studies, it is clear that the combined use of QBD devices, such as RA, detection, experimental design and optimization, facilitates the understanding of the role of the formulation and the process parameters in the quality characteristics of the ODT.[30]

CONCLUSION

In the present review of studies it may conclude that oral disintegrating tablet is an efficient approach as newer drug delivery process as comparison to other conventional drug releasing dosage form. While the selection of the process, material, equipments attributes was used in the development of ODT may carried out by advanced quality embracing tool also called QBD. In the above survey it is found that the ODT formation using quality system became more robust, effective, and free from process errors and also embracing the dosage form design space.

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