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# FORMULATION AND EVALUATION OF PHENYTOIN ORO DISPERSIBLE TABLETS USING VARIOUS SUPER DISINTEGRANTS

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## ABSTRACT

The formulation and evaluation of Phenytoin Oro Dispersible Tablets (ODTs) using super disintegrants aim to improve the dissolution rate and bioavailability of the drug. Phenytoin, an anticonvulsant, is poorly soluble in water, making its oral absorption slow and variable. Oro dispersible tablets offer a practical alternative by rapidly disintegrating in the mouth, enhancing patient compliance and drug release. In this study, various super disintegrants such as cross-linked polyvinylpyrrolidone (Crosprovidone), sodium starch glycolate (SSG) and croscarmellose sodium (CCS) were incorporated into Phenytoin ODT formulations. The tablets were prepared by direct compression method and evaluated for various parameters including hardness, friability, weight variation, content uniformity, disintegration time and *in vitro* drug release. The inclusion of super disintegrants significantly improved the disintegration time, which is a key factor in the rapid onset of action. The formulation with the optimal concentration of cross-linked polyvinylpyrrolidone showed the best drug release profile, with a higher dissolution rate compared to other formulations. The stability of the tablets was also assessed and the formulations exhibited good physical and chemical stability over a specified period. The results indicate that Phenytoin Oro Dispersible Tablets formulated with super disintegrants are an effective dosage form for improving the dissolution and bioavailability of Phenytoin, offering potential benefits for patients who have difficulty swallowing conventional tablets. Further studies are needed to confirm the clinical efficacy and pharmacokinetic profile of these formulations.

## KEYWORDS

Phenytoin, Oro dispersible tablets, Super disintegrants, Crospovidone, Dissolution rate, Bioavailability, Direct compression and Drug release.

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## INTRODUCTION

### Oral solid dosage forms

Drugs can be administered through different routes however, of all the routes of administration, oral route of administration is most convenient for administering drugs for systemic effect because of

ease of administration by manufacturing and dosage adjustments. Oral route of drug administration has wide acceptable.

Oral drug delivery remains the preferred route for administration of various drugs. Recent developments in the technology have prompted scientists to develop orally disintegrating tablets (ODTs) with improved patient compliance and convenience. ODTs are solid unit dosage forms, which disintegrate or dissolve rapidly in the mouth without chewing and water. Orally disintegrating tablets provide an advantage particularly for pediatric and geriatric populations who have difficulty in swallowing conventional tablets and capsules. This review describes the various formulation aspects, disintegrants employed and technologies developed for ODTs, along with various excipients, evaluation tests, marketed formulations, and drugs explored in this field.

**Oro dispersible tablets:**

Over a decade, the demand for development of orally disintegrating tablets (ODTs) has enormously increased as it has significant impact on the patient compliance. Orally disintegrating tablets offer an advantage for populations who have difficulty in swallowing. It has been reported that Dysphagia (difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting, and motion sickness complications. ODTs with good taste and flavor increase the acceptability of bitter drugs by various groups of population.

United States Food and Drug Administration (FDA) defined ODT as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue." The disintegration time for ODTs generally ranges from several seconds to about a minute.

**Significance**

Orally disintegrating tablets offer all advantages of solid dosage forms and liquid dosage forms along with special advantages, which include:

As ODTs are unit solid dosage forms, they provide good stability, accurate dosing, easy manufacturing, small packaging size, and easy to handle by patients.

No risk of obstruction of dosage form, which is beneficial for traveling patients who do not have access to water.

Easy to administer for pediatric, geriatric, and institutionalized patients (specially for mentally retarded and psychiatric patients)

Rapid disintegration of tablet results in quick dissolution and rapid absorption which provide rapid onset of action.

Medication as "bitter pill" has changed by excellent mouth feel property produced by use of flavours and sweeteners in ODTs.

Bioavailability of drugs that are absorbed from mouth, pharynx, and oesophagus is increased.

**Challenges to Develop ODT**

Rapid disintegration of tablet

Avoid increase in tablet size

Have sufficient mechanical strength

Minimum or no residue in mouth

Protection from moisture

Good package design

Compatible with taste masking technology

Not affected by drug properties

**Advantages**

Convenience of administration and accurate dosing as compared to liquids.

No need of water to swallow the dosage from, which is highly convenient feature for patients who are traveling and do not have immediate access to water.

Rapid dissolution of drug and absorption, which may produce rapid onset of action.

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.

**Selection of drugs**

The ideal characteristics of a drug for *in vivo* dissolution from an ODT include

No bitter taste

Dose lower than 20mg

Small to moderate molecular weight
Good stability in water and saliva
Partially non ionized at the oral cavities pH
Ability to diffuse and partition into the epithelium of the upper GIT (logp>1, or preferably>2)
Ability to permeate oral mucosal tissue
Unsuitable drug characteristic for ODT

**Formulation Aspects in Developing ODT**

Orally disintegrating tablets are formulated by utilizing several processes, which differ in their methodologies and the ODTs formed vary in various properties
such as,
Mechanical strength of tablets
Taste and mouth feel
Swallowability
Drug dissolution in saliva
Bioavailability
Stability

**Lyophilization or Freeze-Drying**

Formation of porous product in freeze-drying process is exploited in formulating ODT. Lyophilization is a process, which includes the removal of solvent from a frozen suspension or solution of drug with structure-forming additives. Freeze-drying of drug along with additives imparts glossy amorphous structure resulting in highly porous and lightweight product. The resulting tablet has rapid disintegration and dissolution when placed on the tongue and the freeze- dried unit dissolves instantly to release the drug.

**Molding**

Molding process includes moistening, dissolving, or dispersing the drug with a solvent then molding the moist mixture into tablets (compression molding with lower pressure than conventional tablet compression), evaporating the solvent from drug solution, or suspension at ambient pressure (no vacuum lyophilization), respectively.

**Cotton Candy Process**

This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to ODT.

**Spray Drying**

Highly porous, fine powders are obtained by this method utilized this process for preparing ODT. The ODT formulations consisted of hydrolyzed/unhydrolyzed gelatin as supporting agent for matrix, mannitol as bulking agent, and sodium starch glycolate or croscarmellose sodium as disintegrating agent. Disintegration and dissolution were further improved by adding effervescent components, i.e. citric acid (an acid) and sodium bicarbonate (an alkali). The formulation was spray dried to yield a porous powder. The ODT made from this method disintegrated in <20 s.

**Mass Extrusion**

This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets.

**Compaction**

**Melt granulation**

In this method superpolystate is used as a binder. Superpolystate is a waxy material with an m.p. of 33-37°C and an hydrophilic lipophilic balance of 9. It not only acts as a binder and increases the physical resistance of tablets but also helps the disintegration of tablets as it melts in the mouth and solubilizes rapidly leaving no residue. Super polystate was incorporated in the formulation of ODT by melt granulation method where granules are formed by the molten form of this material.

**Phase transition process**

Tablets were produced by compressing a powder containing two sugar alcohols (erythritol (m.p. 122°C), xylitol (m.p. 93-95°C), trehalose (97°C), and mannitol (166°C)) with high- and low-melting points and subsequent heating at a temperature between their melting points. Before heating

process, the tablets do not have sufficient hardness because of low compatibility. The tablet hardness was increased after heating process, due to the increase of inter particle bonds or the bonding surface area in tablets induced by phase transition of lower melting point sugar alcohol.

**Sublimation**

The presence of a highly porous structure in the tablet matrix is the key factor for rapid disintegration of ODT. Even though the conventional tablets contain highly water-soluble ingredients, they often fail to disintegrate rapidly because of low porosity. To improve the porosity, volatile substances such as camphor can be used in tableting process, which sublimated from the formed tablet.

**Conventional methods**

Conventional methods in formulating tablets such as dry granulation, wet granulation and direct compression methods were adapted to produce ODTs. In formulating ODTs, one of the important components is the super disintegrants. Several excipients are investigated for rapid disintegration of ODTs, some of the super disintegrants employed are discussed here Crosspovidone, Microcrystalline cellulose, sodium starch glycollate, sodium carboxy methyl cellulose, pregelatinized starch, calcium carboxy methyl cellulose, and modified corn starch. Sodium starch glycollate has good flowability than croscarmellose sodium. Cross povidone is fibrous nature and highly compactable.

**Selection of Superdisintegrants**

Factors to be considered for selection of superdisintegrants:

It should produce rapid disintegration (hydrophilic) when tablet meets saliva in the mouth.

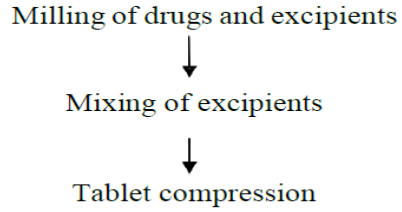
It should be compactable enough to produce less-friable tablets.

It can able to produce good mouth feel to the patient. Thus, small particle size is preferred to achieve patient compliance.

**Direct compression**

In direct compression method the raw materials are size reduced and the required excipients are added and directly compressed. A few crystalline substances call be directly compressed into tablets. Tablet development of lower strength drugs may follow two processes either by traditional alcoholic or aqueous wet granulation technique or via the simple direct compression mode with marginally faster dissolution rates. Dosage strength with 1-l0 mg per 100 or 150 mg tablet is considered suitable drug candidates for direct compression.

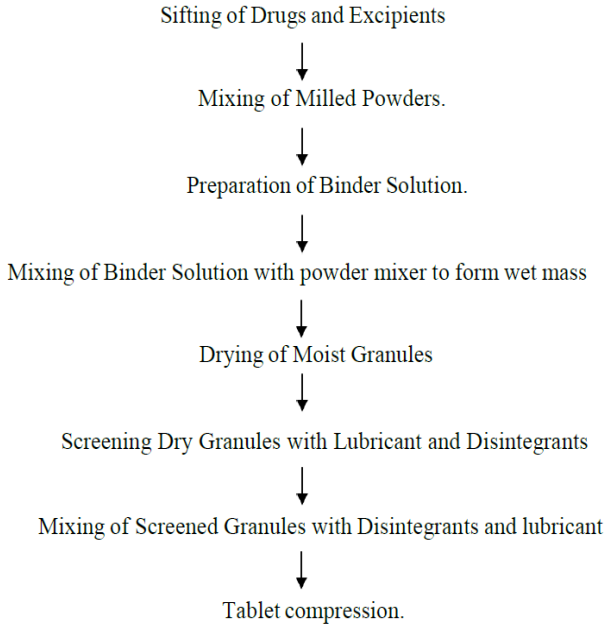
**Main Steps Involved in the direct compression method is**




**Wet granulation**

This is most widely used and the most general method of the tablet preparation. Its popularity is due to the greater possibility that granules will meet all physical requirements for the compression of good tablets. Most powders cannot be compressed directly into tablets because the lack of proper characteristics of binding or together into a compact entity. The donor processes ordinarily lubricated and disintegrating properties.

**Main Steps Involved in the Wet granulation method is**



**Dry granulation**

It is a valuable technique in situations where the effective dose of a drug is too high for direct compaction and the drug is sensitive to heat, moisture, or both, which precludes wet granulation. This method involves the compaction of the components of a tablet formulation by means of a tablet press or specially designed machinery, followed by milling and screening, prior to final compression into tablet. When the initial blend of powders is forced into dies of large capacity tablet press and is compacted by means of flat faced punches, the compacted masses are called "slugs" and the process is referred to as ganslugging". On a large scale, compression granulation.

**Approaches for masking taste**

Orally disintegrating tablet, which disintegrate or dissolve in the saliva and produce a positive or negative taste sensation. Taste is a chemical reaction derived from sensory responses from the four main taste perceptions salt, sour, bitter and sweet. The drugs are mostly bitter in nature. Skillful taste masking is needed to hide the bitter taste in ODT formulations. This can be achieved by using combination of right flavour and right sweeteners. The negative taste sensation of drugs can be reduced or eliminated by various approaches studied, which include addition of sweeteners and flavors, encapsulating the unpleasant drug in to microparticles and adjustment of pH.

**Encapsulation or coating of drugs**

Some of the unpleasant drugs cannot be masked by incorporation of sweeteners and flavors, in such cases alternative method of masking the taste is by encapsulating or coating the drug. In fact this process retards or inhibits dissolution and solubilization of drug, which allows time for particles to pass form mouth before taste is perceived in mouth.

**Various techniques utilized include**

CIMA'S taste masking technique uses coating of drug with dissolution retarding material.

Phase separation approach for taste-masked microcapsules.

Microcaps process used microencapsulation technology.

Extrusion method.

Micromask technology used casting or spin congealing melt dispersions or solution of drug in molten blend of materials.

Flashtab technology.

Solutab technology involves coating drug with sustained release agents, which are finally coated with enteric polymers and further with mannitol.

Blending with cyclodextrins. Cyclodextrins can be used to trap or complex, cyclodextrin help to solubilze many drugs.

OraSolv is other manufacturing technology involves the direct compression of actives effervescent excipients and taste masking agents. Effervescent disintegration agents evolve gas by means of chemical reaction called effervescent couple. The tablet rapidly disintegrates and carbon dioxide is produced by contact with saliva or aqueous fluid. The effervescent excipients are taste masking agents.

Then the excipient is mixed with active ingredient and then compressed into tablets. Carbonates such as sodium bicarbonate, sodium carbonate, potassium bicarbonate and potassium carbonate, magnesium carbonate, acids such as citric, tartaric, amalic, fumeric, adipic and succinies are used.

Dura Solv process is based on Oro-Solv technology, in this non compressible filler along with taste masking excipients and actives used in dry blend then compressed into tablets. Taste masking sweeteners and flavours such as mint, cherry and orange. Drug coating can also be used.

Flash Tab technology is a flash dispersal system which involves coating a drug with a Eudragit polymer (methacrylate copolymer) to provide rapid release of the drug in the stomach, and formulating this microencapsulated drug with an effervescent couple to produce a flash dispersal tablet.

Advatab is a new generation ODT. In this technology the (microcaps- coacervation) microencapsulation process completely envelops individual drug particles with gastro soluble polymer barrier coating between drug and taste

buds in the mouth. Microencapsulation restricts the dissolution of API in the mouth but allow rapid dissolution in the gastro intestinal tract, thus overcoming bioequivalence issues for generic products.

Zydis Technology Zydis formulation is a unique freeze-dried tablet in which drug is physically entrapped or dissolved within the matrix of fast-dissolving carrier material. When zydis units are put into the mouth, the freeze-dried structure disintegrates instantaneously and does not require water to aid swallowing.

WOWTAB Technology WOW means "Without Water ". In this process, combination of low mouldability saccharides and high mouldability saccharides is used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low mouldability saccharide and granulated with a high mouldability saccharide and compressed into tablet.

Flash Dose Technology prepared using flash dose technology is the first commercial product launched by Biovail Corporation. Flash dose tablets consist of self-binding shear form matrix termed as "floss". Shear form matrices are prepared by flash heat processing.

**Patients Who May Benefit from ODTs**

Patients with physical swallowing issues have shown a strong preference for ODTs over conventional tablets. In a crossover study of 36 adult patients with dysphagia, 76% expressed a preference for an ODT . Fewer participants expressed concern over swallowing the ODT than the conventional tablet and only one patient (3%) indicated that they found the ODT “extremely difficult” to swallow, compared with eight patients (21%) who found the conventional tablet “extremely difficult” to swallow.

**Patient counselling in effective use of ODT**

Patient information that needs to be provided includes:

Storage of this dosage form as some of ODT developed may not have sufficient mechanical strength, which needs to be handled carefully.

Patients with Siogren's syndrome or dryness of mouth or who take anticholinergic drugs may not be suitable candidates for administering ODT. Although no water is required to allow drug to disperse quickly and efficiently but decreased volume of saliva may slow the rate of disintegration/dissolution and may reduce the bioavailability of the product.

Patients need to be clearly told about the difference between effervescent and ODT. Some of technologies use effervescence, which experience a pleasing tingling effect on the tongue.

Although chewable tablets are available in market and patient need to be counselled about differences between chewable and ODT tablets. This ODT can be used easily in children who have lost their primary teeth and in geriatric patients who have lost their teeth permanently. With the pharmacists counselling, intervention and assistance about ODT, all patients receiving this novel dosage form could be more properly and effectively treated with greater convenience.

**AIM AND OBJECTIVE**

The main aim of this work was to formulate phenytoin Oro dispersible tablets using various super disintegrants {Crospovidone, Croscarmellose sodium (Ac-do-sol SD-711), Sodium starch glycolate}, Bulking agent {Lactose (Super tab 21AN) Mannitol } Sweetening agent {Aspartame}, Adsorbent { Absil 100 (Silica)} Binding agent { PVP K30} Lubricant {Sodium stearyl fumarate} Pore former {Camphor} by direct compression method and evaluating its characteristics.

Epilepsy is a chronic disorder of the brain that affects people in every country of the world. It is characterized by recurrent seizures.

Epilepsy affects approximately 1% of the population making it one of the most common neurological diseases.

Seizures can vary from the briefest lapses of attention or muscle jerks to severe and prolonged convulsions (i.e. violent and involuntary contractions, or a series of contractions, of the muscles).

Phenytoin is anticonvulsant and antiepileptic drug that binds to specific receptors on neuronal cell membranes it inhibits voltage dependent sodium ion channels to neuronal cell membrane and thus impairs the passage of trains of rapid axon potentials along axons, and it discriminates against epileptic activity.

This or dispersible tablet of Phenytoin will disintegrate rapidly in the patient mouth without need of water or chewing and release its drug content instantaneously.

**Plan of work**

Based on the aim and Objective we had planned to carry out the work based on the flow chart.

To collect literature review.

Collection of raw material

Preparation of blend for direct compression

To conduct preformulating studies for blend prepared

Compression of tablets by direct compression

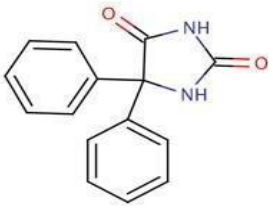
To evaluate the compressed Oro-dispersible tablet

To select the optimized formulation

**Drug profile**

**Phenytoin**

**Structure**




**Category:** Anti convulsant, antiepileptic

**Iupac name:** 5,5-di(phenyl)imidazolidine-2,4-dione

**Molecular formula:** C15H12N2O2

**Molecular weight:** 252.3

**Description**

A white or almost white, crystalline powder, practically insoluble in water, sparingly soluble in alcohol, very slightly soluble in methylene chloride. It dissolves in dilute solutions of alkali hydroxides. An anticonvulsant that is used in a wide variety of seizures. It is also an anti-arrhythmic and a muscle relaxant.

**Pharmacology**

**Mechanism of action**

Phenytoin acts on sodium channels on the neuronal cell membrane, limiting the spread of seizure activity and reducing seizure propagation. By promoting sodium efflux from neurons, phenytoin tends to stabilize the threshold against hyper excitability caused by excessive stimulation or environmental changes capable of reducing membrane sodium gradient. This includes the reduction of post-tetanic potentiation at synapses. Loss of post-tetanic potentiation prevents cortical seizure foci from detonating adjacent cortical areas.

**Indications**

For the control of generalized tonic-clonic (grand mal) and complex partial (psychomotor, temporal lobe) seizures and prevention and treatment of seizures occurring during or following neurosurgery.

**Instructions**

Patients taking phenytoin should be advised of the importance of adhering strictly to the prescribed dosage regimen, and of informing the physician of any clinical condition in which it is not possible to take the drug orally as prescribed, e.g., surgery, etc.

Patients should also be cautioned on the use of other drugs or alcoholic beverages without first seeking the physician's advice.

Patients should be instructed to contact their physician if skin rash develops.

**Toxicity**

Oral, mouse: LD50 = 150 mg/kg; Oral, rat: LD50 = 1635 mg/kg. Symptoms of overdose include coma, difficulty in pronouncing words correctly, involuntary eye movement, lack of muscle coordination, low blood pressure, nausea, sluggishness, slurred speech, tremors, and vomiting.

**Pharmacokinetics**

**Absorption**

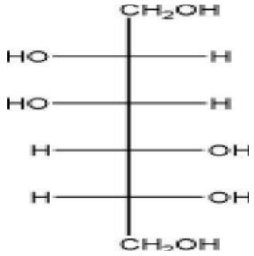
Bioavailability 70-100% oral, 24.4% for rectal and intravenous administration. Rapid rate of absorption with peak blood concentration expected in 1½ to 3 hours.

**Distribution**

Highly protein bound upto 90%.

**Metabolism:** Hepatic metabolism. Metabolized by
Cytochrome P450 3A5 (CYP3A5)
Cytochrome P450 2C19 (CYP2C19)
Cytochrome P450 2C8 (CYP2C8)
Cytochrome P450 2C9 (CYP2C9)
Cytochrome P450 2B6 (CYP2B6)
**Elimination:** Primarily through the bile, urinary
**Half Life:** 6-24 hours
**Storage**
Store in a well-closed container.

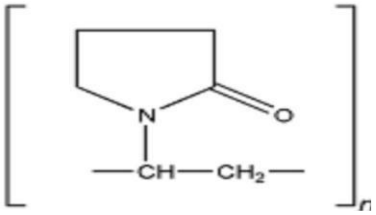
**EXCIPIENT PROFILE**
**MANNITOL**
**Nonproprietary Names**
BP: Mannitol
JP: D-Mannitol
PhEur: Mannitolum
USP: Mannitol
**Synonyms**
Cordycepic acid; *C*PharmMannidex*; E421; manna sugar; D-mannite; mannite; *Mannogem*; *Pearlitol*.
**Chemical Name**
D-Mannitol
**Empirical Formula**
C6H14O6
**Molecular Weight**
182.17
**Structural Formula**




**Functional Category**
Diluent; diluent for lyophilized preparations; sweetening agent; tablet and capsule diluent; tonicity agent**.**
**Description**
Mannitol occurs as a white, odourless, crystalline powder, or free-flowing granules. It has a sweet taste, approximately as sweet as glucose and half as sweet as sucrose and imparts a cooling sensation in the mouth. Microscopically, it appears as orthorhombic needles.
**Applications in Pharmaceutical Formulation or Technology**
Manitol is primarily used as a diluent (10–90% w/w) in tablet formulations,
Mannitol may be used in direct-compression or in wet granulations.
Mannitol is commonly used as an excipient in the manufacture of chewable tablet formulations because of its negative heat of solution, sweetness, and 'mouth feel'.
Mannitol has also been used to prevent thickening in aqueous antacid suspensions.
It has been suggested as a plasticizer in soft-gelatin capsules.
It is used in food applications as a bulking agent.
**Stability and Storage Conditions**
Mannitol is stable in the dry state and in aqueous solutions. The bulk material should be stored in a well-closed container in a cool, dry place.
**Incompatibilities**
Mannitol solutions, 20% w/v or stronger, may be salted out by potassium chloride or sodium chloride. Sodium cephapirin at 2mg/mL and 30mg/mL concentration is incompatible with 20% w/v aqueous mannitol solution. Mannitol is incompatible with xylitol infusion and may form complexes with some metals such as aluminium, copper, and iron. Mannitol was found to reduce the oral bioavailability of cimetidine compared to sucrose.

**CROSPOVIDONE**
**Non-proprietary Names**
BP: Crospovidone
PhEur: Crospovidonum
USPNF: Crospovidone
**Synonyms**
Crosslinked povidone; E1202; *Kollidon CL*; *Kollidon CL-M*; *Polyplasdone XL*; *Polyplasdone XL-10*; polyvinylpolypyrrolidone; PVPP; 1-vinyl-2-pyrrolidinone homopolymer.
**Chemical Name**
1-Ethenyl-2-pyrrolidinone homopolymer

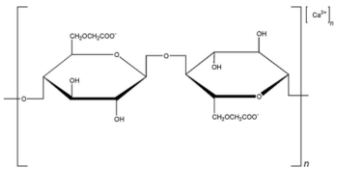
**Empirical Formula**
(C6H9NO)*n*
**Molecular Weight**
>1 000 000
**Structural Formula**



**Functional Category**
Tablet disintegrant.
**Description**
Crospovidone is a white to creamy-white, finely divided, free-flowing, practically tasteless, odourless or nearly odourless, hygroscopic powder.
**Solubility**
Practically insoluble in water and most common organic solvents.
**Applications in Pharmaceutical Formulation or Technology**
Crospovidone is a water-insoluble tablet disintegrant and dissolution agent used at 2–5% concentration in tablets prepared by directcompression or wet- and dry-granulation methods.
Crospovidone can also be used as a solubility enhancer.
With the technique of co-evaporation, crospovidone can be used to enhance the solubility of poorly soluble drugs.
**Stability and Storage Conditions**
Since crospovidone is hygroscopic, it should be stored in an airtight container in a cool, dry place.
**Incompatibilities**
Crospovidone is compatible with most organic and inorganic pharmaceutical ingredients. When exposed to a high-water level, crospovidone may form molecular adducts with some materials.

## CROSCARMELLOSE SODIUM

**Nonproprietary Names**
BP: Croscarmellose sodium
PhEur: Carmellosum natricum conexum
USPNF: Croscarmellose sodium
**Synonyms**
*Ac-Di-Sol*; crosslinked carboxymethylcellulose sodium; *Explocel*; modified cellulose gum; *Nymcel ZSX*; *Pharmacel XL*; *Primellose*; *Solutab*; *Vivasol*.
**Chemical Name**
Cellulose, carboxymethyl ether, sodium salt, crosslinked.
**Empirical Formula**
Croscarmellose sodium is a crosslinked polymer of carboxymethylcellulose sodium.
**Molecular Weight**
90,000- 7,00,000
**Structural Formula**



**Functional Category**
Tablet and capsule disintegrant.
**Description**
Croscarmellose sodium occurs as an odourless, white or greyish-white powder.
**Solubility**
Insoluble in water, although croscarmellose sodium rapidly swells to 4–8 times its original volume on contact with water. Practically insoluble in acetone, ethanol and toluene.
**Applications in Pharmaceutical Formulation or Technology**
Croscarmellose sodium is used in oral pharmaceutical formulations as a disintegrant for capsules, tablets and granules.
In tablet formulations, croscarmellose sodium may be used in both direct compression and wet-granulation processes.
Croscarmellose sodium at concentrations up to 5% w/w may be used as a tablet disintegrant, although normally 2% w/w is used in tablets prepared
by direct compression and 3% w/w in tablets prepared by a wet granulation
process.
**Stability and Storage Conditions**
Croscarmellose sodium is a stable though hygroscopic material.

Croscarmellose sodium should be stored in a well-closed container in a cool, dry place.

**Incompatibilities**

Croscarmellose sodium is not compatible with strong acids or with soluble salts of iron and some other metals such as aluminium, mercury, and zinc.

## SODIUM STARCH GLYCOLATE

**Nonproprietary Names**

BP: Sodium starch glycollate

PhEur: Carboxymethylamylum natricum

USPNF: Sodium starch glycolate

**Synonyms:**

Carboxymethyl starch, sodium salt; *Explosol*; *Explotab*; *Glycolys*; *Primojel*; starch carboxymethyl ether, sodium salt; *Tablo*; *Vivastar P*.

**Chemical Name**

Sodium carboxymethyl starch

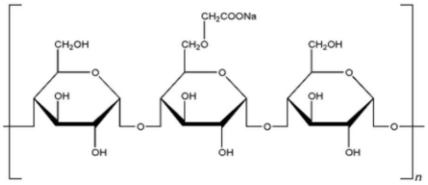
**Empirical Formula**

The USPNF 23 states that sodium starch glycolate is the sodium salt of a carboxymethyl ether of starch, containing 2.8- 4.2% sodium.

**Molecular Weight**

The molecular weight is typically 5 × 105–1 × 106.

**Structural Formula**




**Functional Category**

Tablet and capsule disintegrant.

**Description**

Sodium starch glycolate is a white to off-white, odourless, tasteless, free flowing

powder. It consists of oval or spherical granules, 30–100 μm in diameter, with some less-spherical granules ranging from 10-35μm in diameter.

**Solubility**

Sparingly soluble in ethanol (95%); practically insoluble in water.

**Applications in Pharmaceutical Formulation or Technology**

Sodium starch glycolate is widely used in oral pharmaceuticals as a disintegrant in capsule and tablet formulations.

It is commonly used in tablets prepared by either direct compression or wet-granulation processes.

Sodium starch glycolate has also been investigated for use as a suspending vehicle.

**Stability and Storage Conditions**

Sodium starch glycolate is stable and should be stored in a well-closed container in order to protect it from wide variations of humidity and temperature, which may cause caking.

**Incompatibilities**

Sodium starch glycolate is incompatible with ascorbic acid.

## ASPARTAME

**Nonproprietary Names**

BP: Aspartame

PhEur: Aspartamum

USPNF: Aspartame

**Synonyms**

3-Amino-*N*-(α-carboxyphenethyl)succinamic acid *N*-methyl ester; 3-amino-*N*-(α methoxycarbonylphenethyl)succinamic acid; APM; aspartyl phenylamine methyl ester; *Canderel*; E951; *Equal*; methyl *N*-α-L-aspartyl-Lphenylalaninate; *NutraSweet*; *Pal Sweet*; *Pal Sweet Diet*; *Sanecta*; SC-18862; *Tri-Sweet*.

**Chemical Name**

*N*-α-L-Aspartyl-L-phenylalanine 1-methyl ester

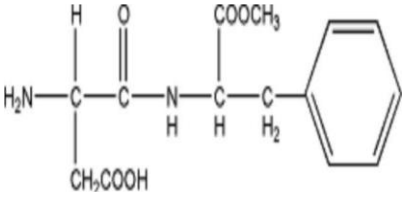
**Empirical Formula**

C14H18N2O5

**Molecular Weight**

294.31

**Structural Formula**



**Functional Category**

Sweetening agent.

**Description**

Aspartame occurs as an off white, almost odourless crystalline powder with an intensely sweet taste.

**Solubility**

Slightly soluble in ethanol (95%); sparingly soluble in water. At 20°C the solubility is 1% w/v at the isoelectric point (pH 5.2).

**Applications in Pharmaceutical Formulation or Technology**

Aspartame is used as an intense sweetening agent in beverage products, food products, and table-top sweeteners, and in pharmaceutical preparations including tablets, powder mixes, and vitamin preparations.

Therapeutically, aspartame has also been used in the treatment of sickle cell anaemia.

**Stability and Storage Conditions**

Aspartame is stable in dry conditions.

The bulk material should be stored in a well-closed container, in a cool, dry place.

**Incompatibilities**

Aspartame is incompatible with dibasic calcium phosphate and also with the lubricant magnesium stearate.

## METHODOLOGY

### Precompression studies

**Bulk density**

Bulk density of a compound various substantially with the method of crystallization, milling or formulation. Bulk density is determined by pouring preserved granules into a graduated cylinder via a large funnel and measure the volume and weight.

$$\text{Bulk density} = \frac{\text{Weight of granules}}{\text{Bulk volume of granules}}$$

**Tapped density**

Tapped density is determined by placing a graduated cylinder containing a known mass of granules and mechanical tapper apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum volume or the percentage of difference is not more than 2%. Using the weight of the drug in the cylinder and this minimum volume, the tapped density may be computed.

$$\text{Tapped density} = \frac{\text{Weight of granules}}{\text{Tapped volume of granules}}$$

**Angle of repose**

Angle of Repose (Φ) is the maximum angle between the surface of a pile of powder and horizontal plane. It is usually determined by Fixed Funnel Method and is the measure of the flowability of powder/granules.

$\theta = \tan^{-1}(h / r)$

Where, h = height of heap of pile

r = radius of base of pile

**Compressibility index**

Compressibility is the ability of powder to decrease in volume under pressure.

Compressibility is a measure that is obtained from density determinations.

$$\% \text{ Compressibility} = \frac{(\text{Tapped density} - \text{Bulk density}) \times 100}{\text{Tapped density}}$$

**Hausner's Ratio**

It is very important parameter to be measured since it affects the mass of uniformity of the dose. It is usually predicted from Hausner Ratio and Angle of Repose Measurement.

$$\text{Hausner Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

**Drug-Excipient Compatibility Study**

Drug is in intimate contact with one or more excipients in all the dosage forms. Later it could affect the stability of drug. Knowledge of drug-excipients interaction is useful in selecting an appropriate excipient. Drug and excipients are stored at 55c for 14 days, 400c at RH 75% for 14 days, 28 days. After 14, 28 days they are subjected for analysis of description, assay, LOD, purity.

**Method of preparation of tablets**

**Direct compression**

In direct compression method the raw materials are size reduced and the required excipients are added and directly compressed. A few crystalline

substances can be directly compressed into tablets. Tablet development of lower strength drugs may follow two processes either by traditional alcoholic or aqueous wet granulation technique or via the simple direct compression mode with marginally faster dissolution rates. Dosage strength with 1-l0 mg per 100 or 150 mg tablet is considered suitable drug candidates for direct compression.

**Main Steps Involved in the direct compression method is**

Milling of drug and excipients

↓

Blending of drug and excipients

↓

Tablet compression

Phenytoin is blended with Micro crystalline cellulose, Pre gelatinized starch and Mannitol.

Shifting of the above mixture through 40 mesh sieve.

Then the above mixture is blended with crospovidone, aspartame, magnesium stearate.

The blended mixture is compressed into tablets.

**Evaluation of compressed tablets**

Tablets from all the formulation were subjected to following quality control test.

**General Appearance**

The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. Include in are tablet's size, shape, colour, presence or absence of an Oduor, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

**Tablet thickness**

Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness is recorded using micrometer. The size of the tablet can be dimensionally described, monitored and controlled.

**Weight variation**

Twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight.

**Disintegration Time**

The test is carried out on the 6 tablets using the apparatus specified in distilled water at $37^{0}$ C ± $2^{0}$ C was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

**Wetting time**

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petridish (ID = 6.5 cm) containing 6 ml of Sorenson's buffer pH 6.8. A tablet was put on the paper and the time for complete wetting was measured. Three trials for each batch were performed and the standard deviation was also determined.

**Friability**

It is measured of mechanical strength of tablets. Roche friabilator is used to determine the friability by following procedure.

Pre weighed tablets are placed in the friabilator. Friabilator consist of a plastic chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets are rotated in the friabilator for at least 4 minutes. At the end of test tablets are dusted and reweighed; the loss in the weight of tablet is the measure of friability and is expressed in percentage as

$$\% \text{ Friability} = \frac{\text{loss in weight / Initial weight X 100}}{}$$

Limits: 0.1-0.9%

**Tablet hardness**

Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation is determined by using Pfizer/Monsato Hardness tester.

IP Limits: 4-10 $kg/cm^2$

**Content uniformity**

Ten randomly selected tablets are weighed and average weight is calculated, the tablets are powdered in a glass mortar. The weight equivalent

to tablet is weighed. The weighed amount is dissolved in solvent system in separate volumetric flask using magnetic stirrer, the volume is adjusted with Sorenson's buffer pH 6.8 and the solution was filtered. An aliquot of these solutions are diluted with Sorenson's buffer pH 6.8 in separate volumetric flasks in Lambert's-Berr's Range. The drug content in formulation is determined spectrophotometrically.

***In vitro* dispersion time**

In vitro dispersion time is measure by dropping a tablet in a beaker containing 50 ml of Sorenson's buffer pH 6.8. Tablets from each batch are randomly selected and invitro dispersion time was performed.

**Fineness of dispersion**

Place 2 tablets in 100ml of water and stir until completely dispersed. Pass the produced smooth dispersion through a sieve screen with a nominal mesh aperture of 710µm.

***In vitro* dissolution studies**

Dissolution study was carried out using USP XXII dissolution test apparatus type II. The dissolution medium was 900ml of 6.8pH phosphate buffer solution, which was maintained at 37±0.5$^0$C. The paddle speed was kept at 50rpm throughout the study. Samples were withdrawn at every 5mins interval of time till 30mins and diluted suitably if required. Further to maintain the sink condition the buffer media was added to the bowl. The samples were analysed spectrophotometrically at 235nm using 6.8pH buffer as blank. The raw dissolution data was analysed for calculating the amount of drug release and percentage cumulative drug released at different time intervals. For finding out the mechanism of drug release from the tablets the dissolution data obtained from

the experiments were treated with the different release kinetic and mechanism

equations.

Medium: 0.05M tris buffer adjusted pH 6.8 with phosphoric acid

Volume: 900 ml

Temperature: 370 + 0.5$^o$c

Apparatus: USP type-2 (paddle)

RPM: 50

Time intervals:5, 10,15, 20, 25 and 30 min

**Preparation of 0.05M tris buffer**

Dissolve 60.5g of tris (hydroxyl methyl) amino methane in 6lts of water. Dilute with water to 10lts and adjust with phosphoric acid to a Ph of 9 ± 0.05. dissolve 100g of sodium lauryl sulphate in about 6lts of prepared buffer, transfer this solution to the remaining buffer solution, and mix.

**Standard preparation**

Dissolve an accurately weighed amount i.e. 60mg of phenytoin in 50ml methanol to obtain a solution having known concentration of 3.0 mg per ml. transfer a portion(5ml) of this solution to a suitable container and dilute quantitatively to 100ml with Dissolution Medium (0.05M Tris buffer) to obtain a concentration of 60ppm. Simultaneously from the above stock solution various concentrations were prepared. These solutions were analysed by using UV spectrophotometer at 229nm.

**Sample preparation**

Place 6 tablets in baskets individually containing 900ml 0.05M Tris buffer which is equilibrated with temperature of 37±0.5ºC at USP paddle 2 apparatus with 50 rpm. At frequent intervals samples are withdrawn from the dissolution medium and replaced with the buffer solution used. The withdrawn samples are diluted if necessary and analysed by using UV spectrophotometer at 229nm.

## RESULTS AND DISCUSSION

**FITR**

Attenuated total reflection-Fourier transform infrared spectrometry (ATR_FTIR) Infrared spectra of samples were recorded in Bruker ATR alpha kept at a ambient temperature of 25.0± 0.5 degree Celsius. The analytical procedure was simple and did not need any special sample preparation. The spectra were recorded by placing the samples on a zinc selenoid crystal plate and screwing the anvel over the sample carefully and scanning the samples in region of 4000-400cm-1 to determine various functional groups. The IR spectrum of the samples was checked for any possible drug excipients

interaction and confirms chemical integrity of Phenytoin in the formulated Oro Dispersible tablets.

Phenytoin is an aromatic amide. For aromatic amides presence of absorption peak between 3400 – 3200 $cm^{-1}$ is characteristic and is due to aromatic nitrogen-hydrogen stretch vibration

Figure No.2 obtained from 'Aldrich library of FT-IR spectra' shows the characteristic vibrations associated with most aromatic amides.

Crospovidone is a polymer of N-vinyl pyrrolidone. Ir spectra of polymers show similar characteristics to their monomeric unit. Hence in spectra of Crospovidone functional vibrations associated with N-vinyl pyrrolidone can be seen. The peak at around 3500$cm^{-1}$ min Crospovidone spectra is associated with C-N stretch. While peak around 1700$cm^{-1}$ is associated with C=O group. Importantly it can be seen that N-H stretch associated with phenytoin remains intact in a binary mixture of Crospovidone and phenytoin.

Sodium starch glycolate is a sodium salt of carboxymethyl starch. The broad peak around 3200 –3500$cm^{-1}$ can be associated with the presence of many alcoholic functional groups. Even in these spectra, the N-H stretch associated with phenytoin can be seen in the spectra of a binary mixture of phenytoin and sodium starch glycolate.

Sodium stearyl fumarate is a sodium salt of the 2-Butenedioic acid, mono-octadecyl ester. The characteristic peak associated with C=O ester group can be seen at around 1700 $cm^{-1}$. The peaks around 2800 cm-1 are associated with C-H stretch. Even in these spectra, the N-H stretch associated with phenytoin can be seen in the spectra of a binary mixture.

Aspartame is salt of the aromatic amino acid. In spectra of aspartame peak of carboxylic acid can be seen around 3400$cm^{-1}$. Peak around 1400$cm^{-1}$ of aromatic C=C can also be seen in aspartame spectra. The peak associated with N-H stretch of phenytoin can be seen in the spectra of a binary mixture.

D-Mannitol is a non-aromatic alcohol. The broad peak at around 3200 $cm^{-1}$ in the spectra of only. D-Mannitol is associated to O-H stretch due to the presence of many -OH groups in the molecule. While the peaks around 1700 $cm^{-1}$ are due to O-H deflections. Also, the peak associated with N-H stretch of phenytoin can be seen in the spectra of a binary mixture. Although the peak is not as sharp as the peak in the spectra of the only phenytoin. This is due to overlapping with the broad peak associated with O-H stretch of D-Mannitol. To resolve the overlapping peaks techniques like deconvolution or Fourier derivation can be employed.

It can be seen that the characteristic peak associated with N-H stretch of phenytoin remains intact in all the spectra's of binary mixtures. It can be concluded that there are no interactions between the excipients used and phenytoin and this further can be considered as a sign of compatibility.

**Interpretation**

The FTIR spectrum confirms the presence of Phenytoin sodium and excipients. The spectrum shows no significant interactions between excipients and API.

**Conclusion**

The FTIR spectrum provides a detailed analysis of the molecular structure of the Phenytoin sodium formulation. The presence of functional groups and spectral regions can be used to identify the API and excipients, and to detect any potential interactions or impurities.

## EVALUTION OF PRE-COMPRESSION STUDIES

**Identification of drug**

The drug sample was evaluated for its Colour, odour and appearance.

**Determination of Powder Characteristics**

**Angle of Repose**

The angle of repose (θ) for each powder was determined by placing the powder in a funnel with the following critical dimensions. Orifice diameter 10mm and base diameter 65mm. The tip of the orifice of the funnel was at fixed height from the ground horizontal surface and the powder was allowed to flow only under the force of gravity.

The angle of repose, θ was calculated from the following relationship. $\tan \theta = h/r$,

Hence, $\theta = \tan^{-1} h/r$

(Where h is height of the pile of powder and r is the radius of the base of cone). $\theta = 35°$

**Bulk Density**

The bulk density was determined by gently pouring the powders into a 100ml volumetric cylinder up to a total volume of 90ml. After weighing the above volume of powder, the bulk density was determined using equation as presented below

Density = Weight (gm)/Volume (ml)

**Tapped density**

It is the ratio of the total mass of the powder (m) to the volume of the powder that is tapped (Vt).

$Dt = m/Vt$

**Compressibility Index (CI)**

The flow ability of powder can be assessed using its bulk (o) and tapped densities (t), as well as the rate at which it compresses.

**Best Flowability**

F6 has the lowest Carr's Index (7.63), indicating excellent flowability. However, it also has the highest standard deviation (1.758), suggesting variability in measurements.

**Worst Flowability**

F4 has the highest Carr's Index (14.84) with a low standard deviation (0.480), indicating consistent but poorer flowability.

**Most Consistent Measurement**

F4 has the smallest standard deviation (0.480), implying highly consistent results.

**Least Consistent Measurement**

F8 has a Carr's Index of 11.51 with the highest standard deviation (2.488), suggesting significant variability.

**Best Flowability**

F8 has the lowest Hausner Ratio (1.07), suggesting excellent flow properties. It has a relatively low standard deviation (0.030), indicating consistent results.

**Worst Flowability**

F4 has the highest Hausner Ratio (1.18), pointing to poorer flowability, but it also has the smallest standard deviation (0.007), suggesting very consistent measurements.

**Most Consistent Measurement**

F4, with a standard deviation of 0.007, shows the most reliable and repeatable results.

**Least Consistent Measurement**

F1 has the highest standard deviation (0.079), implying greater variability in its flowability assessment.

**Lowest LOD**

F1 has the lowest loss on drying (0.27), indicating minimal moisture content, which is favourable for stability and flowability.

**Highest LOD**

F7 has the highest LOD (0.83), suggesting it contains more moisture, which might affect its flow and storage stability.

**General Trend**

Most formulations have LOD values between 0.38 and 0.83, with higher values potentially correlating to formulations with lower flowability, as seen in Carr's Index and Hausner Ratio data.

**Close Values**

F4, F5, and F10 all have LOD values around 0.65-0.66, showing consistency in moisture content.

The LOD data helps evaluate which formulations are more stable and less prone to moisture-related issues, critical for optimizing manufacturing and storage conditions

**Consistent Thickness (Lowest Variability)**

F1 has the most consistent measurements, with minimal differences across tablets (ranging from 4.14 to 4.18mm). Its average is 4.15mm.

F5 also shows consistency with a range of 4.29 to 4.40mm and an average of 4.37mm.

**Largest Thickness (Max Average)**

F6 has the thickest tablets, with an average thickness of 4.53mm, ranging from 4.48 to 4.56mm.

**Smallest Thickness (Min Average)**

F1 has the smallest average thickness (4.15mm), consistent with its tightly grouped measurements.

**Outliers or Variability**

F9 has a wider range of thicknesses (4.11 to 4.42mm) and the largest spread, with an average of 4.26mm. This indicates some variability among its samples.

**Intermediate Thickness (Close Averages)**

Formulations like F3, F7, and F10 fall in the mid-range (averages around 4.33–4.44 mm), showing good control in thickness. This data ensures compliance with quality specifications and helps identify any potential formulation or manufacturing inconsistencies.

**Weight variation**

To check for any weight differences, 20 tablets were randomly selected from each batch and measured independently. The weight of a pill may vary slightly according on the USP. The permitted weight variance percentage deviation is as follows. In all formulations, the weight of the tablet was larger than 200mg, allowing for a maximum variance of 5%.

**Tablet Disintegration**

The table presents disintegration test results (in seconds) for six tablets from each formulation (F1 to F10), evaluated using the Electro lab Disintegration Tester (ED12). Disintegration time is a key quality parameter, ensuring tablets dissolve within the required timeframe for bioavailability.

**Fastest Disintegration (Shortest Average Times)**

F9 disintegrates the fastest, with an average time of approximately 20.92 seconds.

This indicates a quick-release profile suitable for immediate-release tablets.

F10 follows closely, with an average disintegration time of around 21.18 seconds.

**Slowest Disintegration (Longest Average Times)**

F1 has the slowest disintegration, with an average of about 32.46 seconds. This suggests it might be formulated for a slower release or has less optimal tablet properties for quick disintegration.

F6 also takes longer, averaging about 23.62 seconds.

**Consistent Disintegration Times (Low Variability)**

F7 demonstrates consistent disintegration times, ranging from 21.14 to 22.14 seconds.

F8 and F4 also show tight ranges, with minimal variation among their tablets.

Formulations with Slight Variability

F1 exhibits the widest range in disintegration times (from 31.42 to 33.93 seconds), indicating some inconsistency in the formulation or manufacturing process.

**Wetting time**

F8 appears to be the best-performing formulation in terms of wetting time, with the lowest and most consistent values.

F1 has the highest wetting times, indicating it takes the longest.

F10 has highly variable wetting times, which might indicate inconsistency in formulation or testing conditions.

**Friability**

For F3, consider increasing binder concentration or adjusting compression force to improve durability.

For the best-performing formulations (F7, F8), consistency should be maintained in the manufacturing process.

**Tablet hardness**

**Highest Hardness**

F7 and F9 show the highest average hardness (3.46 and 3.42Kg/cm²) with upper values approaching 3.98–3.99Kg/cm².

**Most Consistent**

F8 has the narrowest range (3.00–3.49Kg/cm²), suggesting strong uniformity in tablet production.

**Potential Issues**

F5 demonstrates the widest range (3.03–3.99Kg/cm²), indicating a need for better control over compression parameters.

***In vitro* dissolution studies**

Invitro dissolution study was performed by using USP dissolution testing apparatus 2 (Paddle method). Weighed tablets from different batches were kept in a flask of the dissolution apparatus containing 900ml of pH 6.8 Phosphate buffer dissolution medium maintained at 37 ± 0.5ºC and at a speed of 50rpm. Aliquot of dissolution medium was withdrawn at specific time intervals, and the samples were replaced with fresh dissolution medium. Aliquot were analysed spectrophotometrically at 235nm against Suitable blank using UV-visible spectrophotometer.

All formulations meet the required specifications for drug content.

F2, F8 and F10 demonstrate the least variability, indicating high consistency in manufacturing.

F3 and F4 show the highest variability, suggesting potential factors affecting uniformity (e.g., blending or distribution inconsistencies).

**Solubility studies**

The solubility of phenytoin sodium was determined by dissolving the highest unit dose of the drug in 500mL of buffer adjusted to pH 6.8buffer and kept in rotary shaker for 48 hrs. Later on, the insoluble drug was filtered off, and the solution was analysed by UV technique at 235nm to find out the solubility. Later on, based on the absorbance value the solubility was calculated.

A graph is plotted with concentration on X-axis and absorbance on Y-axis. There was a straight line.

**Table No.1: Excipients commonly used for ODT preparation**

| S.No | Name and weight percentage of different excipients Name of excipients | Percentage used |
|---|---|---|
| 1 | Disintegrant | 1 to 15% |
| 2 | Diluents | 0 to 85% |
| 3 | Binder | 5 to 10% |
| 4 | Antistatic Agent | 0 to 10% |

**Pharmacology**

**Table No.2: Mechanism of action**

| Side Effects | |
|---|---|
| Neurologic | Nystagmus, ataxia, opthalmoparesis, sedation, allergic reactions. |
| Hematologic | Megaloblastic anemia, agranulocytosis, aplastic anemia, leucopenia, thrombocytopenia. |
| Teratogenicity | Craniofacial anomalies, mental retardation |
| Gingival | Hyperplasia |
| Dermatologic | Hypertrichosis, rash, exfoliative dermatitis, pruritis. |
| Auto immune disease | Stevens-Johnson syndrome (SJS) and toxic epidermalnecrolysis (TEN) |

**Table No.3: Dosage forms**

| S.No | Form | Route |
|---|---|---|
| 1 | Capsule | Oral |
| 2 | Liquid | Intramuscular |
| 3 | Liquid | Intravenous |
| 4 | Solution | Intramuscular |
| 5 | Suspension | Oral |
| 6 | Tablet | Oral |

**Table No.4: Solubility- Solubility of Mannitol**

| S.No | Solvent | Solubility at 20°C |
|---|---|---|
| 1 | Alkalis | Soluble |
| 2 | Ethanol (95%) | 1 in 83 |
| 3 | Ether | Practically insoluble |
| 4 | Glycerin | 1 in 18 |
| 5 | Propan-2-ol | 1 in 100 |
| 6 | Water | 1 in 5.5 |

**Table No.5: Drug-Excipient Compatibility Study**

| S.No | Ingredients | Ratio | Description | | |
|---|---|---|---|---|---|
| | | | Initial | 55ºC 14 days | 40ºC and 75% 28 days |
| 1 | Phenytoin sodium | 1:0 | White Powder | NCC | NCC |
| 2 | Drug+Lactose (Supertab 21AN) | 1:4 | White Powder | NCC | NCC |
| 3 | Drug+Absil 100 (Silica) | 1:1 | White Powder | NCC | NCC |
| 4 | Drug + mannitol | 1:4 | White crystalline powder | NCC | NCC |
| 5 | Drug + crospovidone | 1:1 | White Powder | NCC | NCC |
| 6 | Drug + Ac-do-sol SD-711 | 1:1 | White crystalline powder | NCC | NCC |
| 7 | Drug + sodium starch glycolate | 1:1 | White crystalline powder | NCC | NCC |
| 8 | Drug + aspartame | 1:0 | Red Colour Powder | NCC | NCC |
| 9 | Drug + PVP K30 | 1:1 | White Powder | NCC | NCC |
| 10 | Drug + Camphor | 1:1 | White Powder | NCC | NCC |
| 11 | Drug + Sodium stearyl fumerate | 1:1 | White Semisolid | NCC | NCC |

**Table No.6: Formulation design of different batches of Oro dispersible tablets of phenytoin**

| S.No | Ingredients | Category/ Uses | Concentration (mg) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 |
| 1 | Phenytoin sodium | API | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| 2 | Crospovidone | Super disintegrant | -- | 10 | 20 | -- | -- | -- | -- | 20 | -- | -- |
| 3 | Croscarmellose sodium (Ac-do-sol SD-711) | | -- | -- | -- | 10 | 20 | -- | -- | -- | 20 | -- |
| 4 | Sodium starch glycolate | | -- | -- | -- | -- | -- | 10 | 20 | -- | -- | 20 |
| 5 | Lactose (Supertab 21AN) | Bulking agent | 80 | 80 | 80 | 83 | 80 | 83 | 80 | 70 | 70 | 70 |
| 6 | Mannitol | | 63 | 53 | 43 | 50 | 43 | 50 | 43 | 43 | 43 | 43 |
| 7 | Aspartame | Sweetening agent | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| 8 | Absil 100 (Silica) | Adsorbent | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 9 | PVP K30 | Binding agent | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 10 | Sodium stearyl fumerate | Lubricant | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| 11 | Camphor | Pore former | -- | -- | -- | -- | -- | -- | -- | 10 | 10 | 10 |
| Total weight of the tablet | | | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |

**Table No.7: Weight variation**

| S.No | Average weight of tablets | % deviation |
|---|---|---|
| 1 | 130 or less | 10 |
| 2 | >130-<324mg | 7.5 |
| 3 | >324mg | 5 |

**Table No.8: Physiochemical properties**

| S.No | Description | Values |
|---|---|---|
| 1 | Formula | C15H12N2O2 |
| 2 | Molecular Weight (MW) | 252.27 g/mol |
| 3 | No.Heavy atoms | 19 |
| 4 | Odour | Odourless |
| 5 | Colour | White |
| 6 | Melting Point | 295-298 degree Celsius |
| 7 | No.H-bond acceptors | 2 |
| 8 | No.H-bond donors | 2 |
| 9 | Solubility | >37.8 [ug/mL] (The mean of the results at pH 7.4) |
| 10 | Stability | Sensitive to Light |

**Table No.9: Angle of Repose**

| Angle of Repose | | | |
|---|---|---|---|
| **Formulation No** | **Radius (r) cm** | **Height (h) cm** | **Angle of repose tan θ=h/r** |
| F1 | 5.5 | 2.87 | 27.53 |
| F2 | 5.3 | 2.98 | 29.32 |
| F3 | 5.1 | 2.78 | 28.68 |
| F4 | 5.5 | 3.06 | 29.06 |
| F5 | 5.4 | 2.66 | 26.30 |
| F6 | 5.2 | 2.65 | 27.00 |
| F7 | 5.1 | 2.94 | 29.28 |
| F8 | 5.4 | 3.12 | 29.76 |
| F9 | 5.5 | 3.18 | 29.50 |
| F10 | 5.4 | 3.12 | 29.90 |

**Table No.10: Angle of Repose**

| S.No | Angle of Repose (θ) | Powder Flow |
|---|---|---|
| 1 | <25 | Excellent |
| 2 | 25-30 | Good |
| 3 | 30-40 | Passable |
| 4 | >40 | Very poor |

**Table No.11: Bulk Density**

| Bulk density | | |
|---|---|---|
| **Formulation No** | **Measuring cylinder** | **Standard Deviation** |
| F1 | 0.40 | 0.001 |
| F2 | 0.41 | 0.002 |
| F3 | 0.39 | 0.004 |
| F4 | 0.42 | 0.002 |
| F5 | 0.43 | 0.005 |
| F6 | 0.45 | 0.004 |
| F7 | 0.38 | 0.004 |
| F8 | 0.43 | 0.001 |
| F9 | 0.46 | 0.004 |
| F10 | 0.45 | 0.007 |

**Table No.12: Tapped density**

| Tapped density | | |
|---|---|---|
| **Formulation No** | **Tapped density** | **Standard deviation** |
| F1 | 0.447 | 0.006 |
| F2 | 0.477 | 0.008 |
| F3 | 0.462 | 0.010 |
| F4 | 0.495 | 0.004 |
| F5 | 0.468 | 0.000 |
| F6 | 0.483 | 0.007 |
| F7 | 0.436 | 0.013 |
| F8 | 0.459 | 0.010 |
| F9 | 0.529 | 0.005 |
| F10 | 0.523 | 0.000 |

**Table No.13: Compressibility Index (CI)**

| S.No | Flow Ability | Carr's Index | Hausner's Ratio |
|---|---|---|---|
| 1 | Excellent | 0 – 10 | 1.00 – 1.11 |
| 2 | Good | 10 – 15 | 1.12 – 1.18 |
| 3 | Fair | 16 – 20 | 1.19 – 1.25 |
| 4 | Passable | 21 – 25 | 1.26 – 1.34 |
| 5 | Poor | 26 – 30 | 1.35 – 1.45 |

**Table No.14: Carr's Index**

| Carr's Index | | |
|---|---|---|
| **Formulation No** | **Carr's Index** | **Standard deviation** |
| F1 | 9.52 | 1.144 |
| F2 | 14.06 | 1.123 |
| F3 | 14.69 | 1.340 |
| F4 | 14.84 | 0.480 |
| F5 | 8.68 | 1.260 |
| F6 | 7.63 | 1.758 |
| F7 | 12.35 | 1.256 |
| F8 | 11.51 | 2.488 |
| F9 | 12.73 | 1.540 |
| F10 | 14.56 | 1.277 |

**Table No.15: Hausner Ratio**

| Hausner ratio | | |
|---|---|---|
| **Formulation No** | **Hausner ratio** | **Standard deviation** |
| F1 | 1.11 | 0.079 |
| F2 | 1.16 | 0.016 |
| F3 | 1.17 | 0.038 |
| F4 | 1.18 | 0.007 |
| F5 | 1.10 | 0.015 |
| F6 | 1.08 | 0.008 |
| F7 | 1.14 | 0.022 |
| F8 | 1.07 | 0.030 |
| F9 | 1.15 | 0.020 |
| F10 | 1.17 | 0.018 |

**Table No.16: Loss on drying**

| Loss on drying | | |
|---|---|---|
| **Formulation No** | **Loss on drying** | **Standard deviation** |
| F1 | 0.27 | 0.060 |
| F2 | 0.45 | 0.054 |
| F3 | 0.38 | 0.029 |
| F4 | 0.66 | 0.042 |
| F5 | 0.66 | 0.070 |
| F6 | 0.75 | 0.082 |
| F7 | 0.83 | 0.063 |
| F8 | 0.71 | 0.099 |
| F9 | 0.72 | 0.022 |
| F10 | 0.65 | 0.038 |

**Table No.17: Tablet thickness**

| **Formulation** | **Thickness (mm) using Mitutoyo vernier caliper** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **Tablet numbers** | | | | | | | |
| | **1** | **2** | **3** | **4** | **5** | **6** | **Average** | **Stdev** |
| F1 | 4.15 | 4.18 | 4.15 | 4.14 | 4.15 | 4.16 | 4.15 | 0.015 |
| F2 | 4.31 | 4.30 | 4.30 | 4.33 | 4.42 | 4.43 | 4.35 | 0.060 |
| F3 | 4.32 | 4.34 | 4.30 | 4.34 | 4.33 | 4.35 | 4.33 | 0.018 |
| F4 | 4.45 | 4.44 | 4.40 | 4.43 | 4.40 | 4.44 | 4.43 | 0.022 |
| F5 | 4.38 | 4.37 | 4.40 | 4.37 | 4.29 | 4.38 | 4.37 | 0.038 |
| F6 | 4.48 | 4.52 | 4.55 | 4.56 | 4.53 | 4.51 | 4.53 | 0.029 |
| F7 | 4.33 | 4.32 | 4.35 | 4.34 | 4.41 | 4.42 | 4.36 | 0.043 |
| F8 | 4.48 | 4.44 | 4.46 | 4.47 | 4.48 | 4.46 | 4.47 | 0.015 |
| F9 | 4.11 | 4.14 | 4.18 | 4.20 | 4.22 | 4.42 | 4.26 | 0.022 |
| F10 | 4.34 | 4.33 | 4.35 | 4.43 | 4.40 | 4.44 | 4.44 | 0.030 |

**Table No.18: Weight variation**

| Formulation | Weight variation (%) (Rad-wag semi micro balance (Model-AS82/220. R2) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Tablet numbers | | | | | | | | | | |
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Average weight |
| F1 | 202.72 | 200.35 | 202.23 | 200.72 | 202.84 | 204.69 | 202.13 | 201.12 | 202.23 | 200.24 | 201.93 |
| F2 | 204.57 | 200.23 | 204.34 | 205.66 | 202.28 | 202.78 | 204.00 | 205.55 | 203.11 | 203.27 | 203.58 |
| F3 | 202.32 | 202.49 | 202.32 | 202.44 | 201.88 | 201.84 | 202.45 | 203.99 | 201.62 | 201.47 | 202.28 |
| F4 | 202.36 | 201.24 | 204.21 | 202.40 | 201.48 | 201.49 | 202.21 | 202.41 | 201.29 | 200.22 | 201.93 |
| F5 | 200.37 | 202.21 | 204.39 | 200.98 | 200.17 | 200.38 | 202.45 | 203.79 | 200.96 | 203.00 | 201.87 |
| F6 | 201.61 | 202.78 | 203.33 | 202.40 | 200.54 | 201.40 | 202.08 | 202.03 | 203.79 | 202.10 | 202.21 |
| F7 | 201.28 | 201.20 | 200.35 | 202.47 | 202.68 | 200.72 | 203.02 | 202.65 | 203.90 | 201.32 | 201.96 |
| F8 | 200.00 | 202.00 | 200.00 | 202.00 | 201.00 | 204.00 | 204.48 | 203.05 | 202.10 | 203.30 | 202.19 |
| F9 | 202.72 | 200.35 | 202.23 | 200.72 | 202.84 | 204.69 | 202.13 | 201.12 | 202.23 | 200.24 | 201.93 |
| F10 | 204.57 | 200.23 | 204.34 | 205.66 | 202.28 | 202.78 | 204.00 | 205.55 | 203.11 | 203.27 | 203.58 |

**Table No.19: Tablet Disintegration**

| Formulation | Disintegration test using electro lab disintegration tester (ED12) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Seconds | | | | | | | |
| | 1 | 2 | 3 | 4 | 5 | 6 | Average | Stdev |
| F1 | 32.88 | 33.93 | 33.65 | 31.42 | 32.90 | 32.00 | 32.80 | 0.955 |
| F2 | 22.22 | 23.67 | 22.96 | 22.21 | 21.98 | 23.36 | 22.73 | 0.697 |
| F3 | 20.56 | 21.45 | 21.87 | 22.00 | 20.18 | 20.99 | 21.18 | 0.727 |
| F4 | 22.29 | 23.14 | 23.18 | 23.76 | 22.00 | 21.77 | 22.69 | 0.784 |
| F5 | 19.76 | 20.59 | 20.85 | 21.03 | 19.78 | 21.52 | 20.59 | 0.703 |
| F6 | 23.33 | 23.72 | 23.24 | 23.44 | 22.60 | 23.38 | 23.29 | 0.373 |
| F7 | 21.14 | 22.14 | 21.88 | 21.16 | 21.82 | 21.61 | 21.63 | 0.405 |
| F8 | 22.45 | 23.02 | 22.13 | 21.76 | 21.59 | 22.00 | 22.16 | 0.517 |
| F9 | 23.33 | 23.72 | 23.24 | 23.44 | 21.82 | 21.61 | 21.63 | 0.606 |
| F10 | 21.14 | 22.14 | 21.88 | 21.16 | 22.60 | 23.38 | 23.29 | 0.772 |

**Table No.20: Wetting time**

| Formulation | Wetting time | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Seconds | | | | | | | |
| | 1 | 2 | 3 | 4 | 5 | 6 | Average | Stdev |
| F1 | 11.30 | 10.77 | 10.22 | 10.00 | 11.65 | 11.43 | 10.90 | 0.677 |
| F2 | 9.12 | 9.46 | 8.88 | 9.49 | 9.68 | 9.60 | 9.37 | 0.308 |
| F3 | 8.33 | 8.45 | 9.12 | 9.64 | 9.00 | 8.78 | 8.89 | 0.479 |
| F4 | 8.65 | 8.21 | 8.00 | 7.94 | 8.45 | 9.05 | 8.38 | 0.423 |
| F5 | 6.65 | 7.00 | 7.43 | 6.98 | 6.96 | 7.11 | 7.02 | 0.252 |
| F6 | 7.53 | 7.32 | 7.98 | 7.14 | 7.24 | 7.77 | 7.50 | 0.327 |
| F7 | 6.16 | 6.43 | 6.00 | 5.85 | 6.14 | 6.23 | 6.14 | 0.198 |
| F8 | 5.56 | 5.58 | 5.99 | 5.00 | 5.34 | 5.76 | 5.54 | 0.342 |
| F9 | 7.53 | 7.32 | 7.98 | 7.14 | 6.14 | 6.23 | 6.14 | 0.532 |
| F10 | 5.58 | 5.99 | 5.00 | 5.34 | 8.45 | 9.05 | 6.38 | 0.722 |

**Table No.21: Friability**

| Friability | | | |
|---|---|---|---|
| **Formulation** | **Initial Weight (mg)** | **Final Weight (mg)** | **Friability** |
| F1 | 200 | 198.5 | 0.75 |
| F2 | 200 | 199 | 0.5 |
| F3 | 200 | 197.8 | 1.1 |
| F4 | 200 | 198.8 | 0.6 |
| F5 | 200 | 199.2 | 0.4 |
| F6 | 200 | 198 | 1 |
| F7 | 200 | 199.5 | 0.25 |
| F8 | 200 | 199.3 | 0.35 |
| F9 | 200 | 198.7 | 0.65 |
| F10 | 200 | 198.2 | 0.9 |

**Table No.22: Tablet hardness**

| **Formulation** | **(Hardness Kg/cm$^2$) using B39 tablet hardness tester** | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Tablet numbers** | | | | | | | | | | | |
| | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **Average** | **Stdev** |
| F1 | 3.44 | 3.39 | 3.00 | 3.20 | 3.32 | 3.12 | 3.36 | 3.24 | 3.44 | 3.56 | 3.31 | 0.17 |
| F2 | 3.50 | 3.02 | 3.00 | 3.18 | 3.55 | 3.02 | 3.35 | 3.18 | 3.03 | 3.35 | 3.23 | 0.20 |
| F3 | 3.00 | 3.24 | 3.47 | 3.53 | 3.55 | 3.61 | 3.36 | 3.45 | 3.38 | 3.39 | 3.40 | 0.18 |
| F4 | 3.00 | 3.23 | 3.27 | 3.28 | 3.27 | 3.45 | 3.43 | 3.20 | 3.34 | 3.52 | 3.30 | 0.15 |
| F5 | 3.14 | 3.17 | 3.99 | 3.98 | 3.33 | 3.08 | 3.12 | 3.03 | 3.19 | 3.04 | 3.31 | 0.37 |
| F6 | 3.68 | 3.25 | 3.18 | 3.05 | 3.51 | 3.53 | 3.20 | 3.25 | 3.18 | 3.96 | 3.38 | 0.28 |
| F7 | 3.34 | 3.98 | 3.94 | 3.10 | 3.19 | 3.23 | 3.16 | 3.33 | 3.68 | 3.66 | 3.46 | 0.33 |
| F8 | 3.00 | 3.39 | 3.33 | 3.28 | 3.39 | 3.22 | 3.29 | 3.49 | 3.30 | 3.03 | 3.27 | 0.15 |
| F9 | 3.34 | 3.98 | 3.94 | 3.10 | 3.19 | 3.27 | 3.45 | 3.43 | 3.20 | 3.34 | 3.45 | 0.22 |
| F10 | 3.08 | 3.18 | 3.55 | 3.02 | 3.35 | 3.12 | 3.36 | 3.24 | 3.44 | 3.56 | 3.22 | 0.32 |

**Table No.23: Percentage Drug content**

| Formulation | % Drug content using 6.8pH phosphate buffer |
|---|---|
| 1 | 99.25 ± 1.06 |
| 2 | 97.18 ± 0.55 |
| 3 | 98.11 ± 1.47 |
| 4 | 100.02 ±1.36 |
| 5 | 101.00 ±0.94 |
| 6 | 96.33 ± 1.00 |
| 7 | 98.14 ± 1.08 |
| 8 | 95.55± 0.77 |
| 9 | 97.99±1.14 |
| 10 | 98.00±0.66 |

**Table No.24: Calibration graph of Phenytoin**

| 6.8 pH Buffer | | | | | |
|---|---|---|---|---|---|
| **Concentration (µg/mL)** | **Absorbance 1** | **Absorbance 2** | **Absorbance 3** | **Average** | **Stdev** |
| 0 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| 10 | 0.121 | 0.147 | 0.114 | 0.127 | 0.017 |
| 20 | 0.202 | 0.232 | 0.192 | 0.209 | 0.021 |
| 30 | 0.307 | 0.287 | 0.317 | 0.304 | 0.015 |
| 40 | 0.399 | 0.429 | 0.382 | 0.403 | 0.024 |
| 50 | 0.520 | 0.520 | 0.511 | 0.517 | 0.005 |
| 60 | 0.629 | 0.611 | 0.635 | 0.625 | 0.012 |
| 70 | 0.733 | 0.720 | 0.742 | 0.732 | 0.011 |
| 80 | 0.800 | 0.838 | 0.822 | 0.820 | 0.019 |
| 90 | 0.910 | 0.918 | 0.925 | 0.918 | 0.008 |
| 100 | 0.996 | 0.998 | 0.998 | 0.997 | 0.001 |

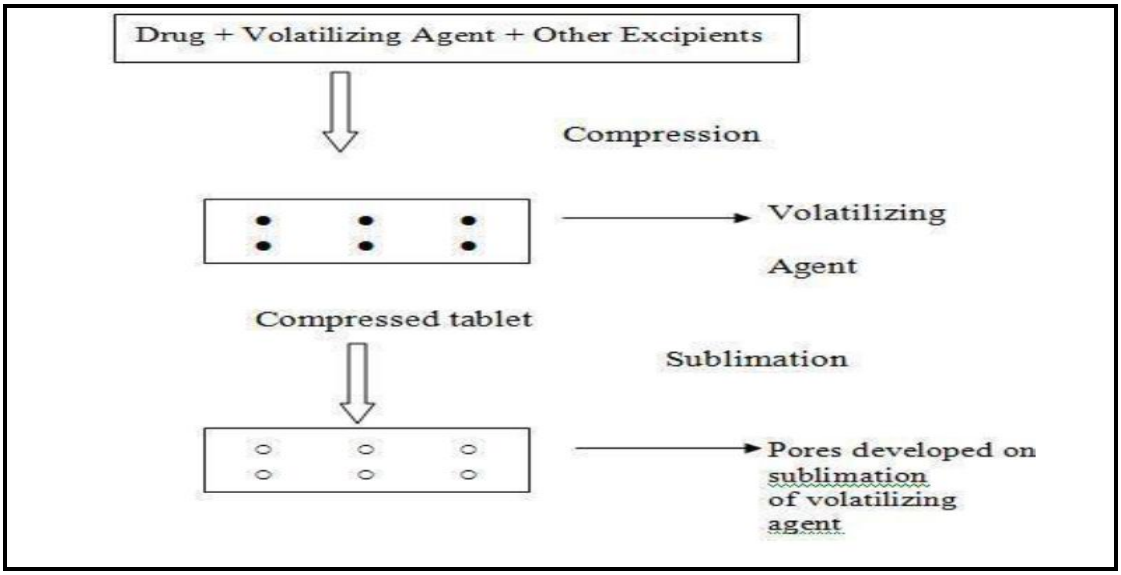



**Figure No.1: Sublimation**

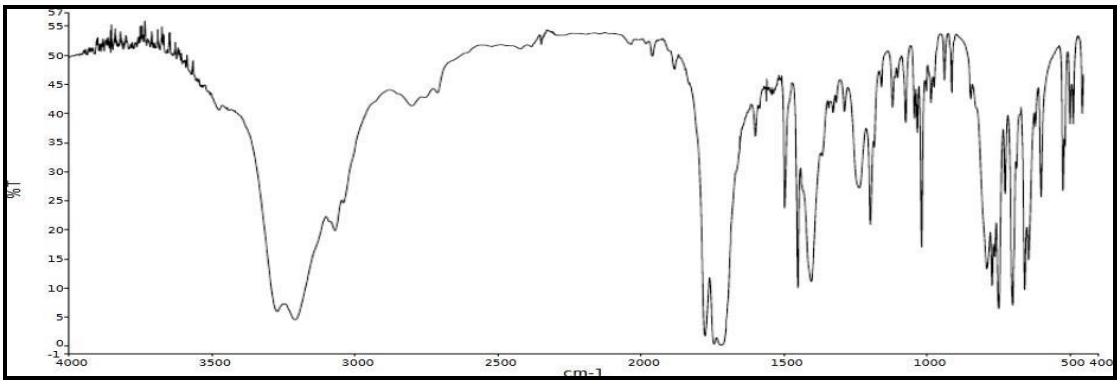



**Figure No.2: FTIR of Phenytoin sodium**

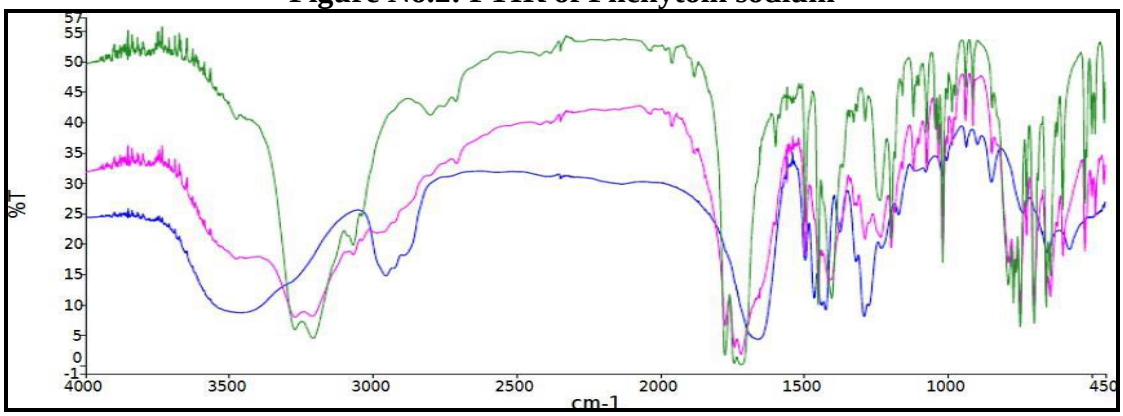



**Figure No.3: Phenytoin and Crospovidone compatibility FT-IR spectra**

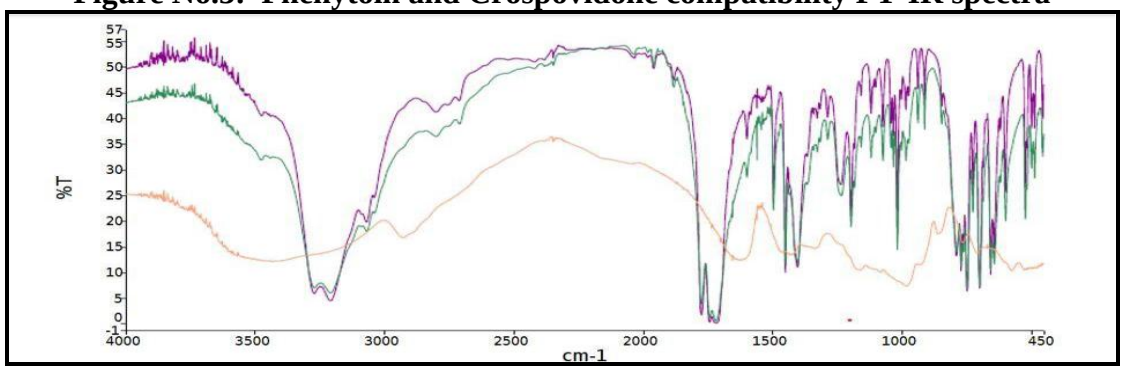



**Figure No.4: Phenytoin + Sodium starch glycolate binary mixture FT-IR spectra**

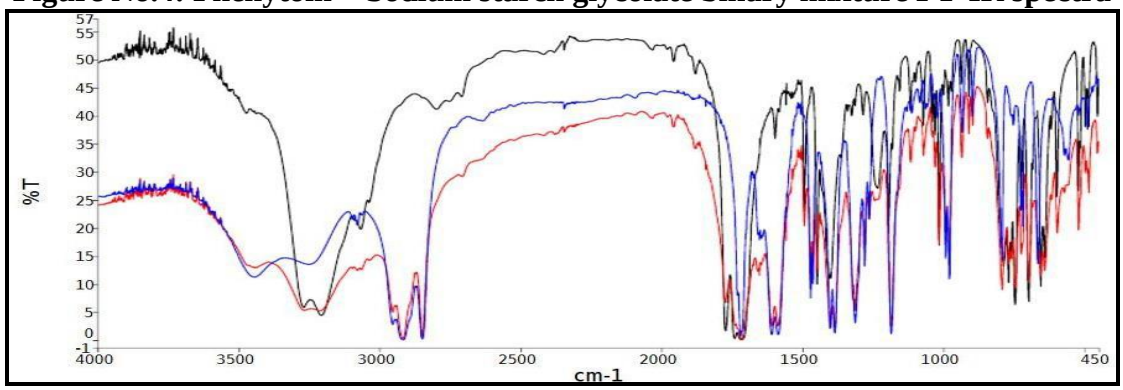



**Figure No.5: Phenytoin + Sodium stearyl fumarate binary mixture FT-IR spectra**

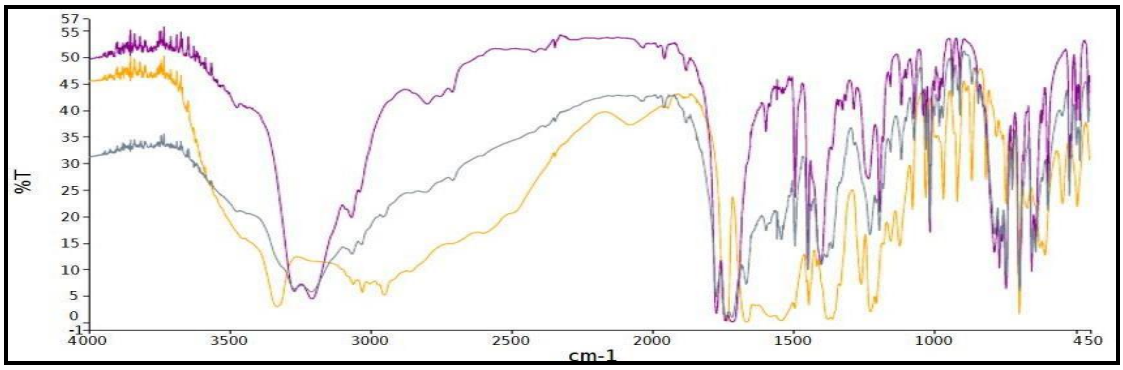



**Figure No.6: Phenytoin + Aspartame binary mixture FT-IR spectra**

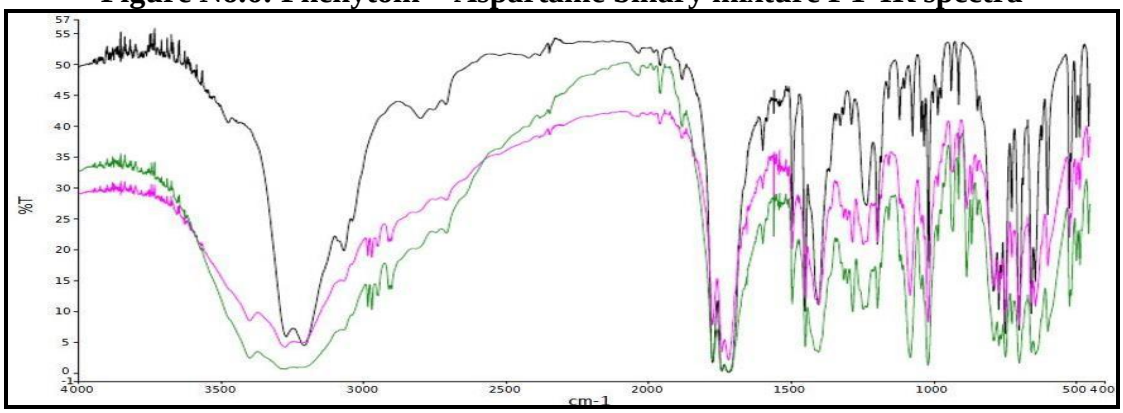



**Figure No.7: Phenytoin + D-Mannitol binary mixture FT-IR spectra**

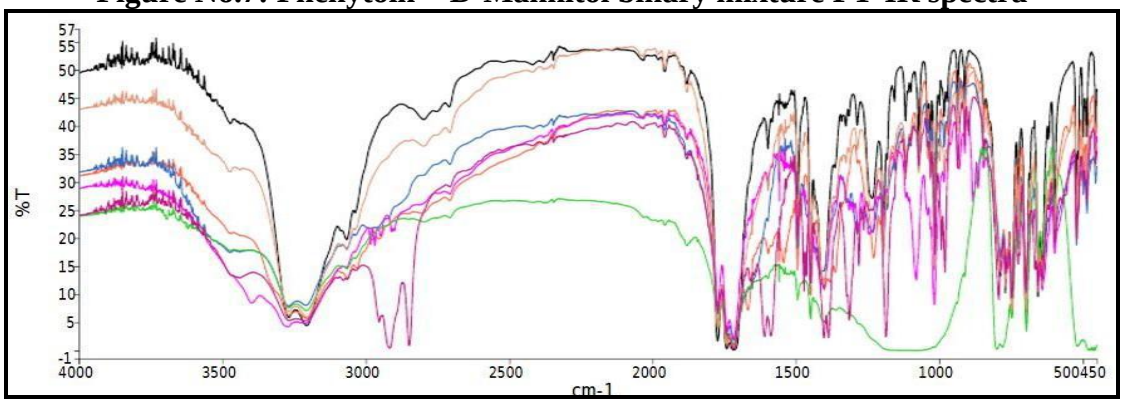



**Figure No.8: Phenytoin + all excipients binary mixture FT-IR spectra**

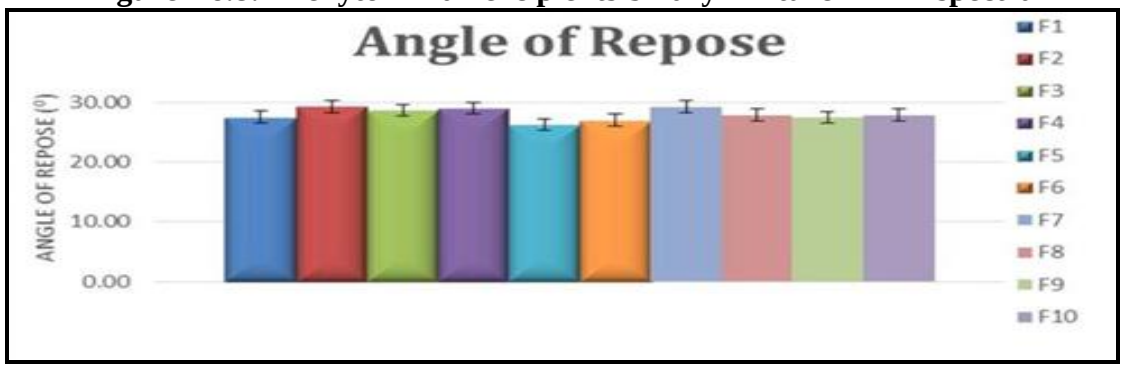



**Figure No.9: Angle of Repose**

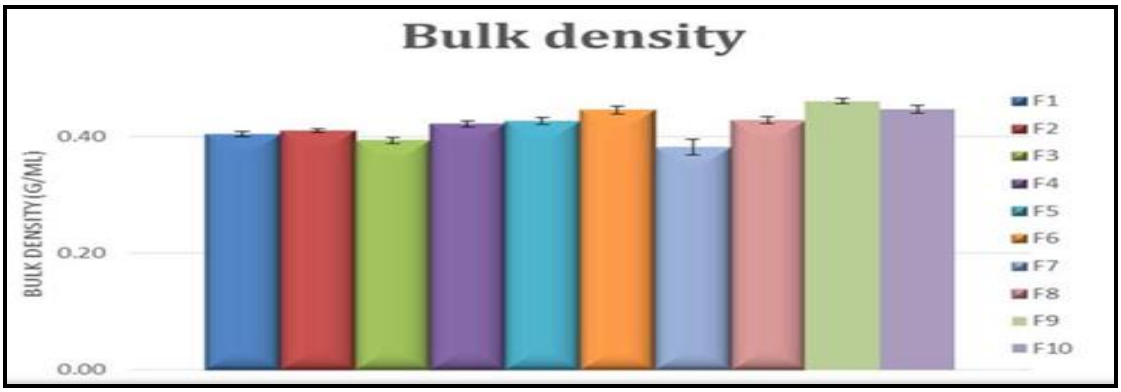



**Figure No.10: Bulk Density**

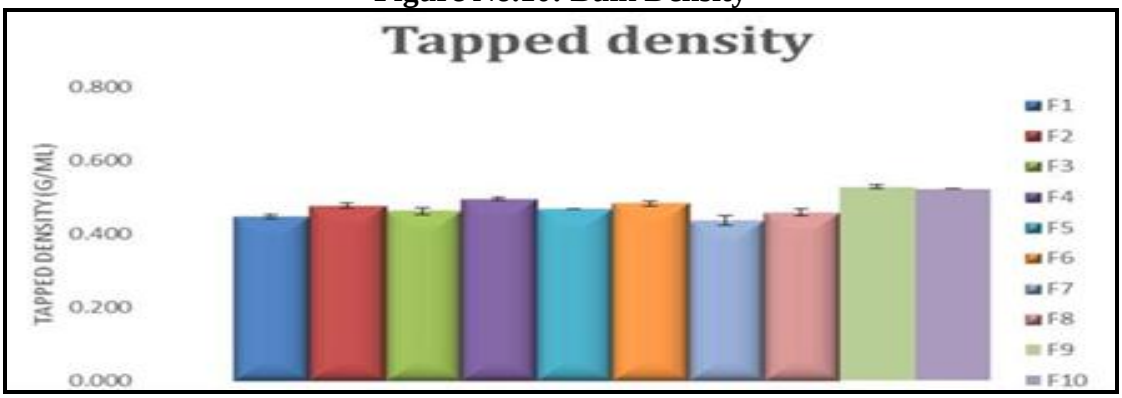



**Figure No.11: Tapped Density**

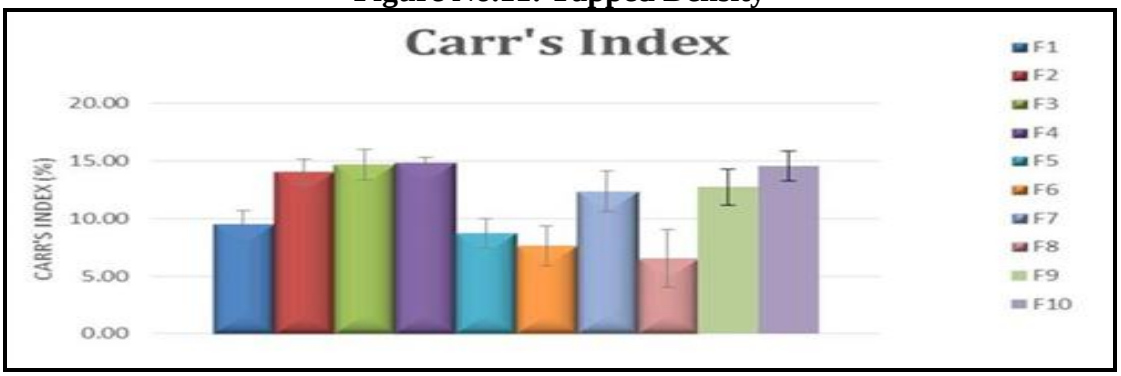



**Figure No.12: Carr's Index**

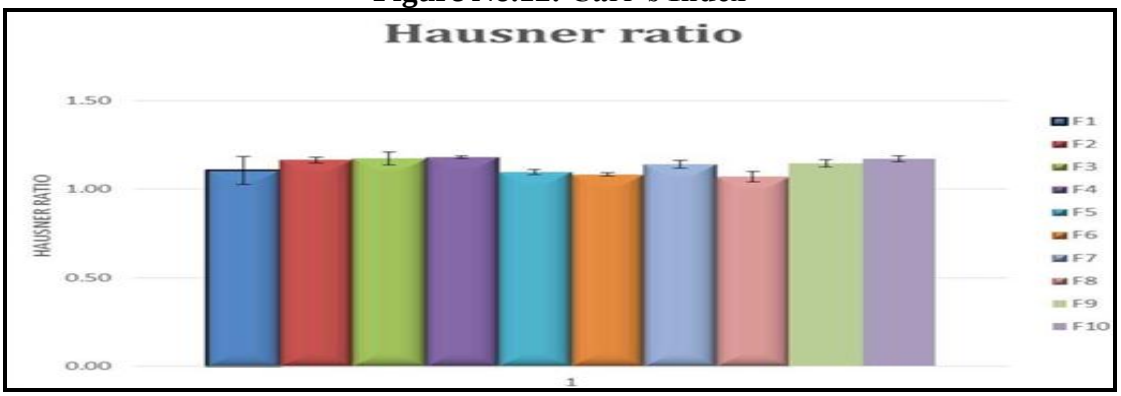



**Figure No.13: Hausner Ratio**

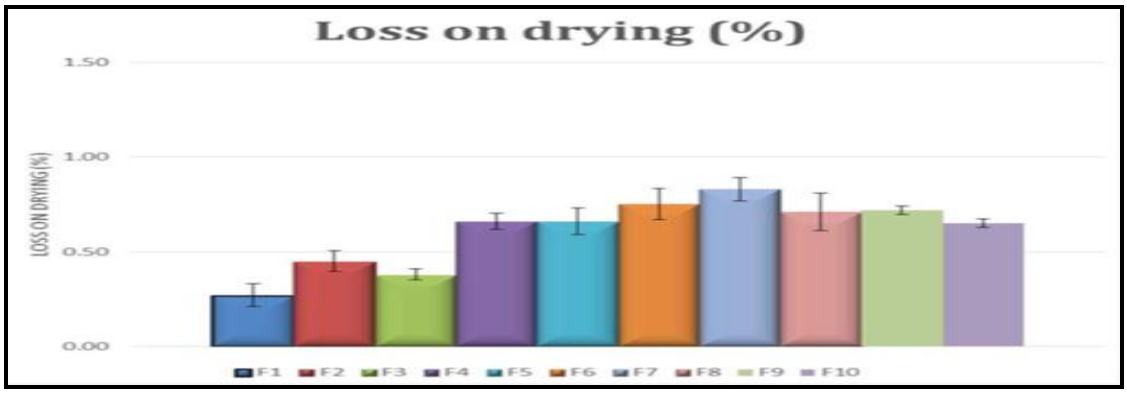



**Figure No.14: Loss on Drying**

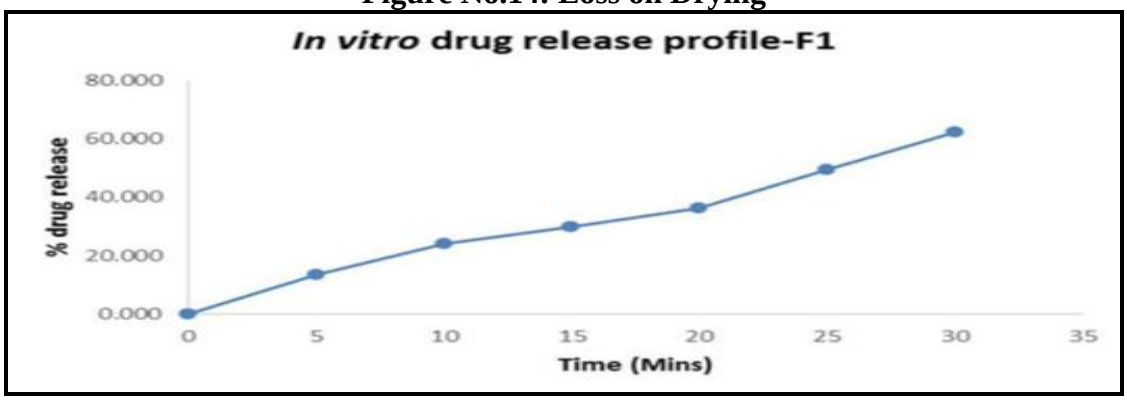



**Figure No.15: *In vitro* drug release profile - F1**

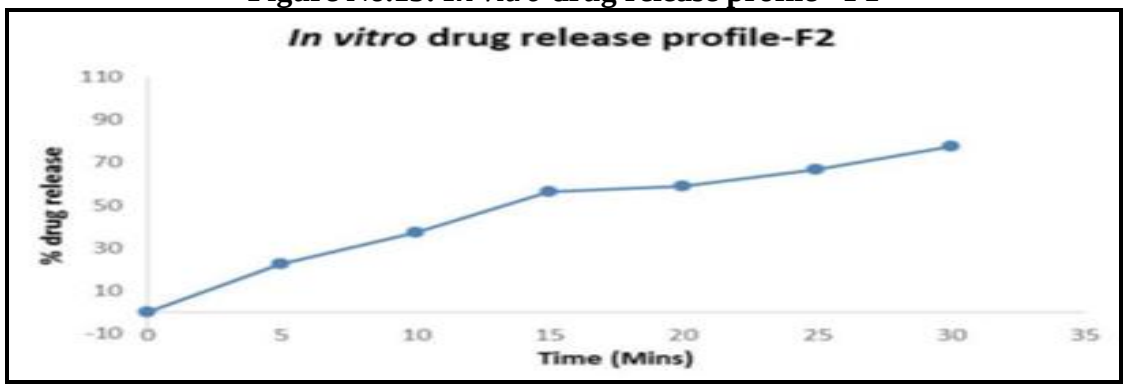



**Figure No.16: *In vitro* drug release profile – F2**

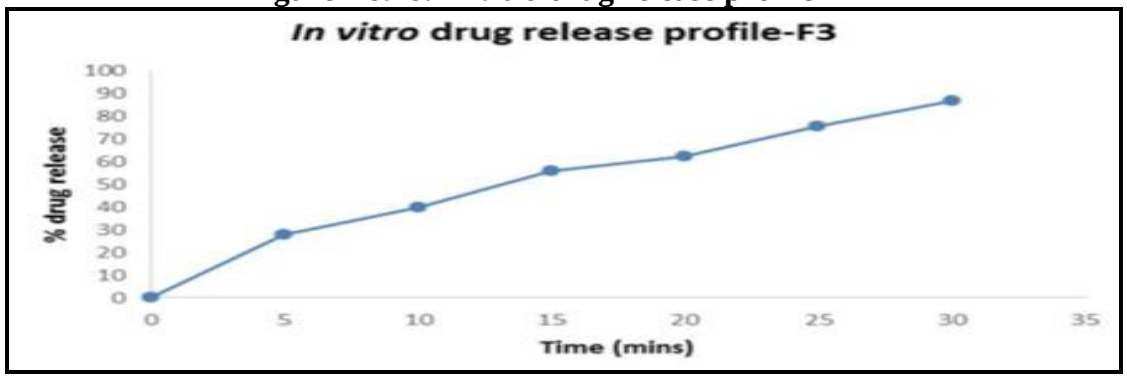



**Figure No.17: *In vitro* drug release profile – F3**

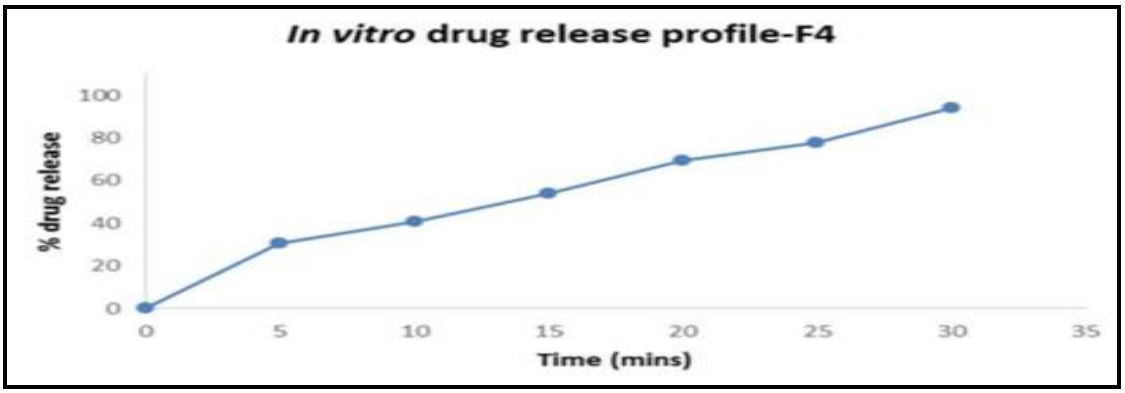



**Figure No.18: *In vitro* drug release profile – F4**

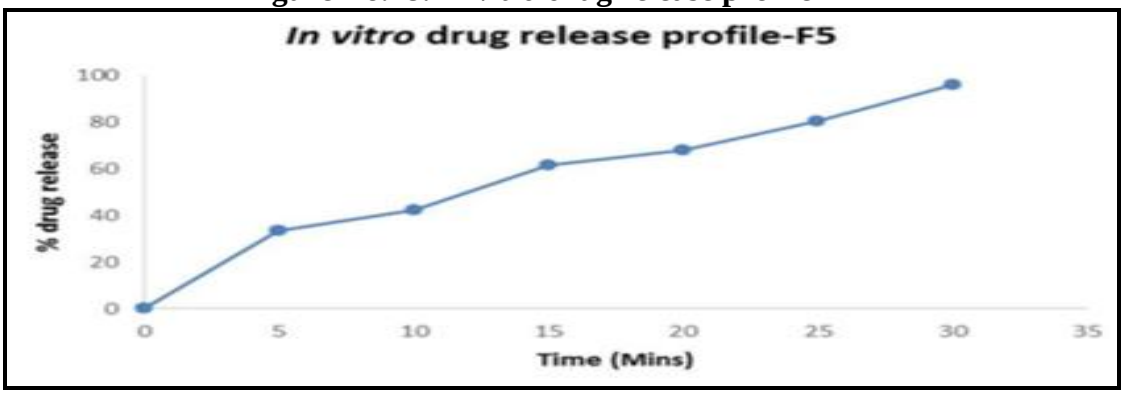



**Figure No.19: *In vitro* drug release profile – F5**

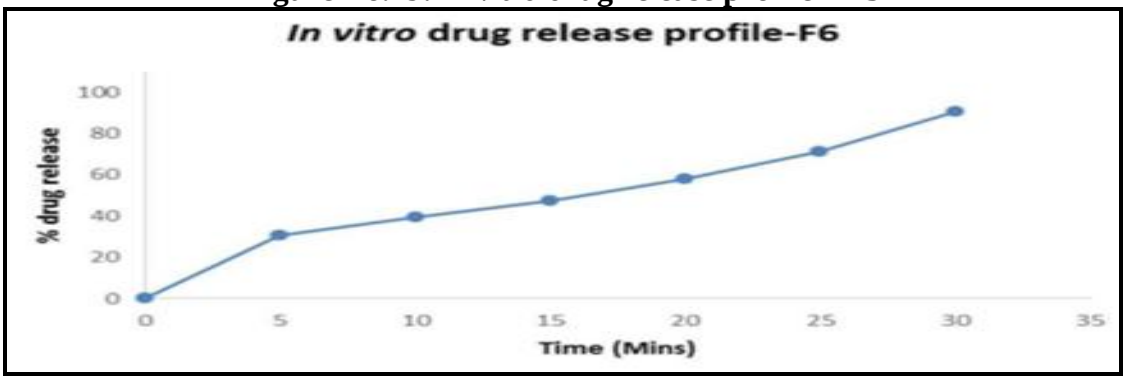



**Figure No.20: *In vitro* drug release profile – F6**

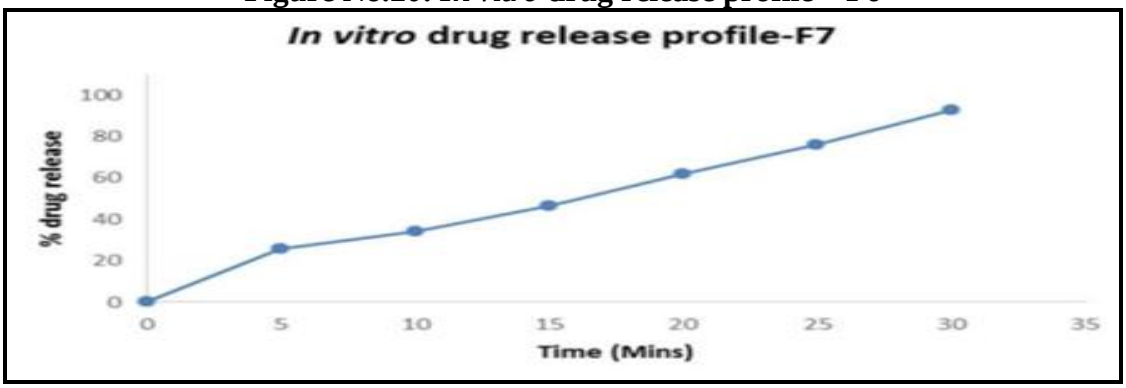



**Figure No.21: *In vitro* drug release profile – F7**

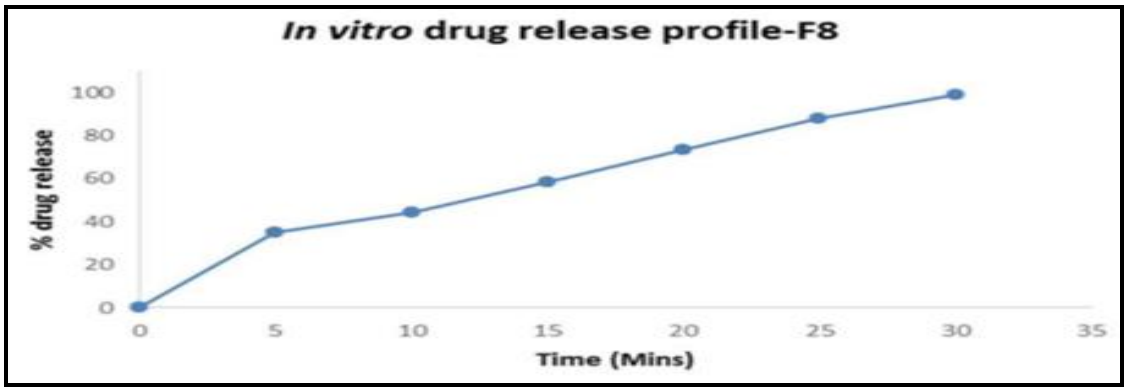



**Figure No.22: *In vitro* drug release profile – F8**

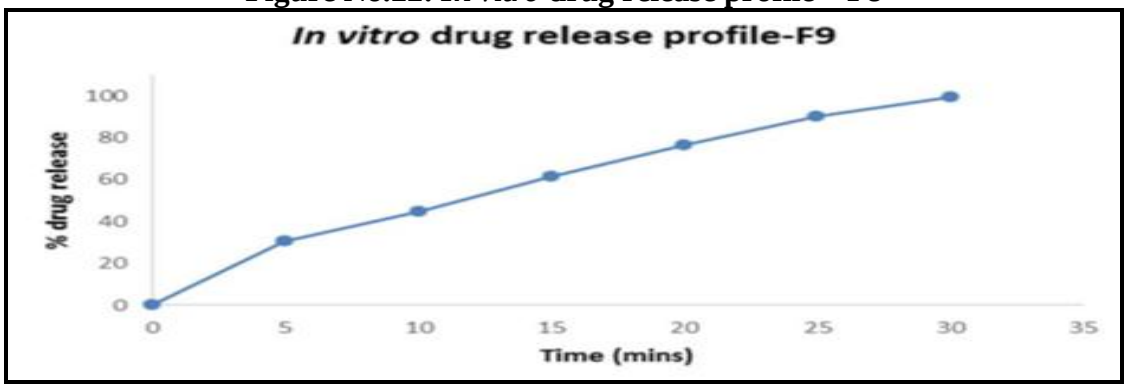



**Figure No.23: *In vitro* drug release profile – F9**

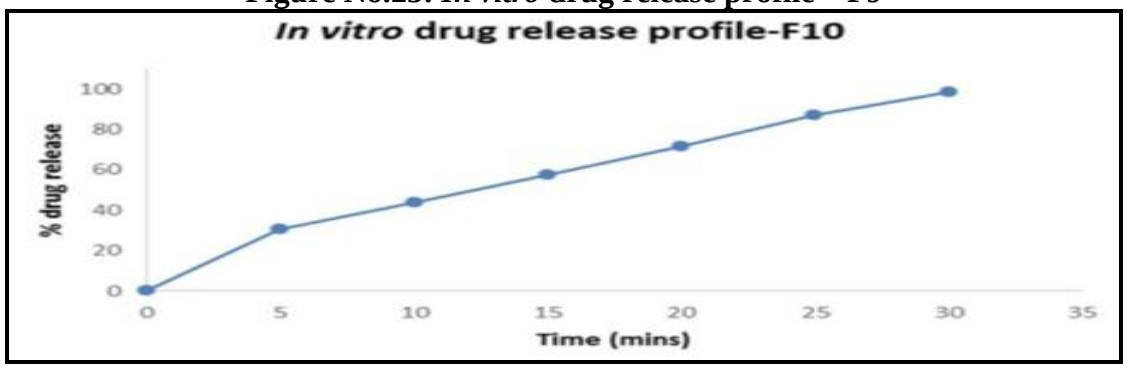



**Figure No.24: *In vitro* drug release profile – F10**

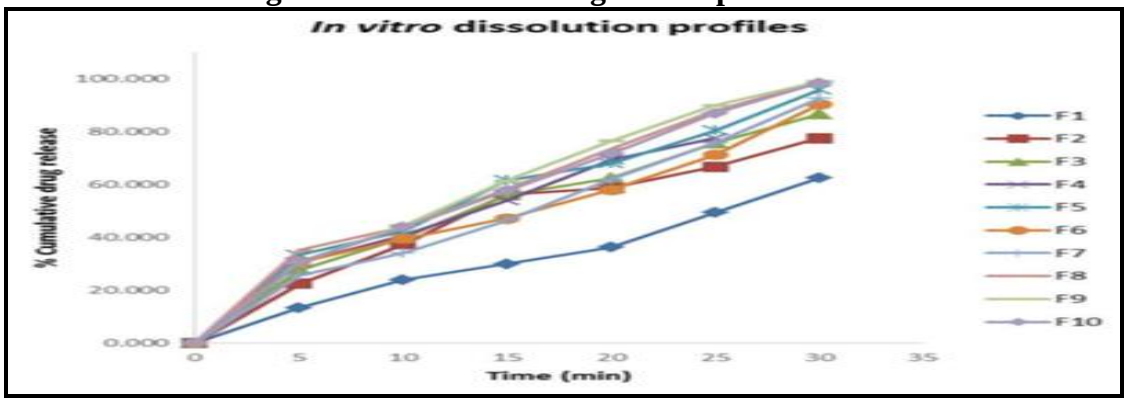



**Figure No.25: *In vitro* drug release profile - Zero order Kinetics**

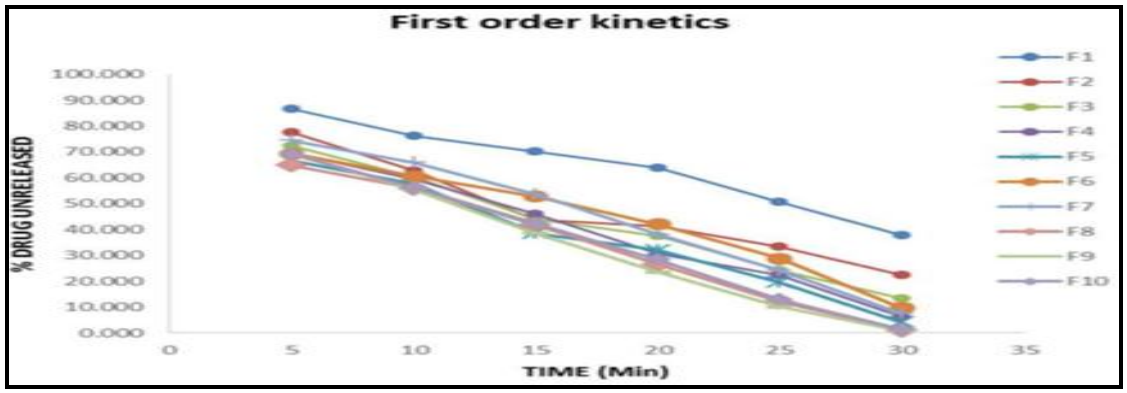



**Figure No.26: *In vitro* drug release profile - First order Kinetics**

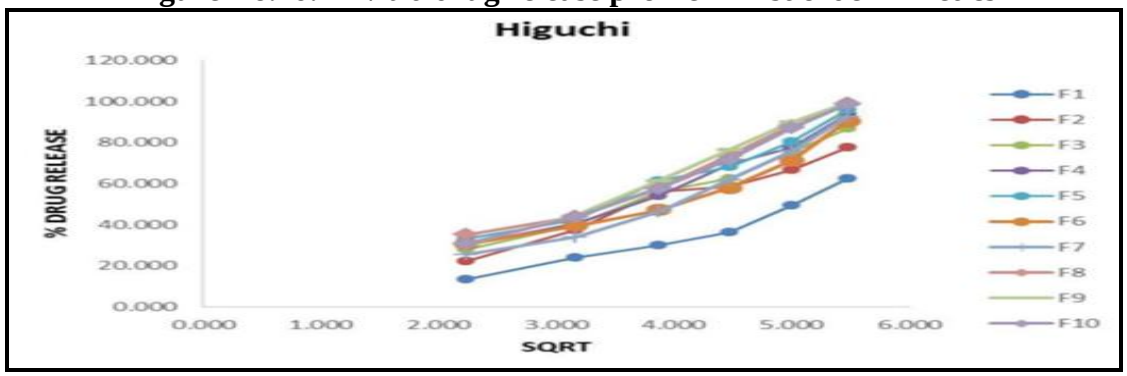



**Figure No.27: *In vitro* drug release profile – Higuchi plot**

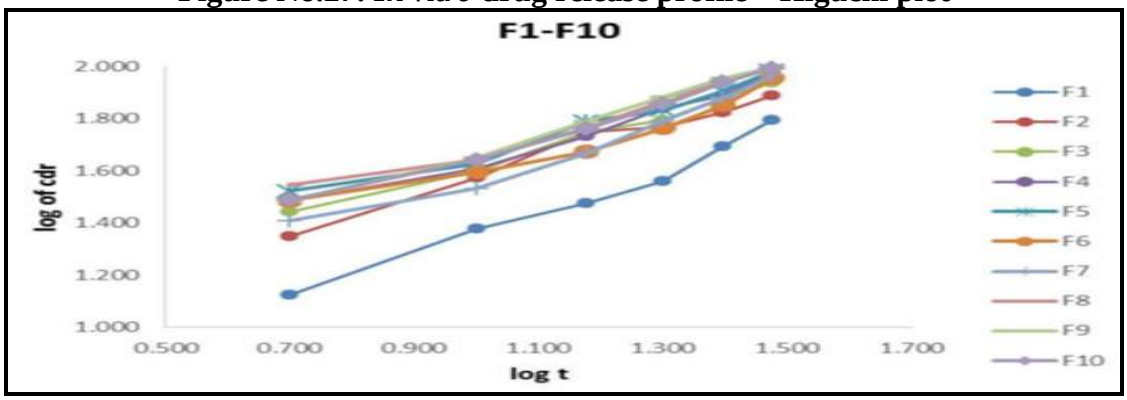



**Figure No.28: *In vitro* drug release profile – PEPPAS plot**

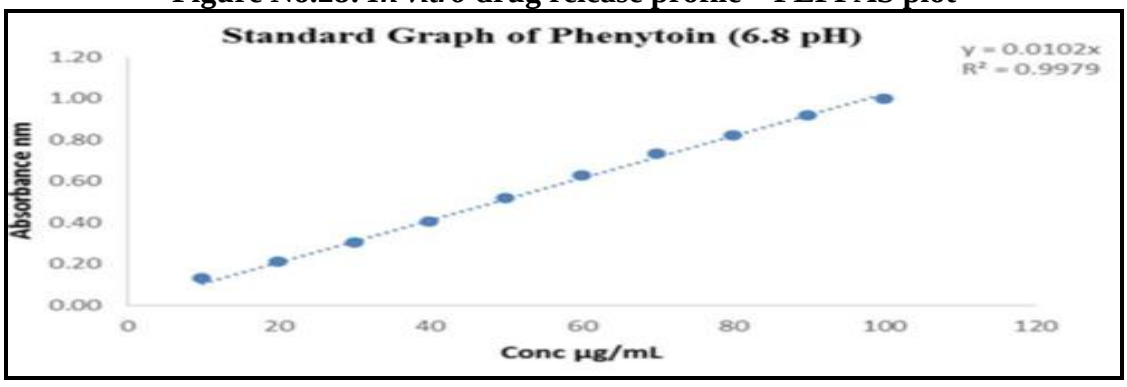



**Figure No.29: Standard graph of Phenytoin**

## SUMMARY AND CONCLUSION

Phenytoin is anticonvulsant and antiepileptic drug that binds to specific receptors on neuronal cell membranes it inhibits voltage dependent sodium ion channels to neuronal cell membrane and thus impairs the passage of trains of rapid axon potentials along axons and it discriminates against epileptic activity.

The present study is looking forward to develop ODT formulation for Phenytoin by simple and less consuming Direct compression method. The concept of formulating Oro dispersible tablets containing Phenytoin offers a suitable approach in serving desired objective of faster disintegration and dissolution characteristics with increased bioavailability.

Drug-Excipient compatibility studies were performed and observations have showed API-excipients does not show any colour changes and they were similar to the initial samples. Hence all the excipients used in the study were found compatible with the API.

The pre compression parameters such as Bulk density, tapped density, Angle of repose, Compressibility index and Hausner's ratio were conducted which showed good granular nature and good flow properties for blend for compression. A total of 10 formulations were prepared by using different super disintegrants of different concentrations by Direct compression method. Post compression parameters such as weight variation, hardness, thickness, disintegration time, wetting time, friability were performed and all the parameters complies with the specifications of Oro dispersible tablets.

F2, F3 and F8 were formulated with different concentrations of Crospovidone (1.5%, 3%, 5%) F4, F5 and F9 were formulated with different concentrations of Croscarmellose sodium (Ac-Di-sol SD-711) (1.5%, 3%, 5%), F6, F7 and F10 were formulated with different concentrations of Sodium starch glycolate, F1 was formulated with Pure drug.

In all these 10 formulations F8 to F10 is considered as the optimized batch as it shows best results compared to all other formulations.

The addition of the super disintegrate at different concentration enhanced the disintegration time of tablets, significantly further the disintegration time was still more enhanced by the addition of Camphor.

In turn leading to enhancement in the dissolution profile of Phenytoin Sodium formulation.

Pre compression parameters for the optimized batch F8 to F10 were like Bulk density (0.43gm/cm3), Tapped density (0.58gm/cm3), Angle of repose (32.51), Compressibility index (18.26%) and Hausner's ratio (1.29).

The F8 to F10 was optimized with various tablet parameters like Thickness (5.38mm), Hardness (4.6kg/m2), disintegration time (25sec), friability (0.586%), which were the limits. The dissolution showed high % drug release with in 25minutes.

The conclusion within of overall study suggests that Oro dispersible tablets of phenytoin can be formulated by direct compression method which in turn provides patient convenience of taking the medication without water and also quick onset of action due to rapid dissolution of the dosage form.

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## CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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