Introduction:

The oral routes of drug administration is the most used route, comparing to other routes, for the delivery of drug to systemic effect, by different dosage forms using different pharmaceutical products. Due to ease of transportability, comparatively low manufacturing cost and does not require sterile manufacturing condition, seems to be most popular in the conventional tablet formulations [Vishwakarma et al., (2011)]. To attain such popularity for solid oral dosage forms the administered drug is well absorbed in the form of stuffs of food that are daily ingested in spite of inherent constraints of GI physiology of oral drug delivery systems are subjected for varying extents of optimization for dosage form characteristics. Hence, it is very much essential to understand the fundamentals of different disciplines, including the pharmacodynamics, pharmacokinetics gastrointestinal physiology and the formulation design which in turn helps to develop an oral pharmaceutical dosage forms successfully. The approach of sophisticated multiple disciplines yield much complexity in the design and optimization of the system. The well understanding of aspects such as pharmacokinetic, pharmacodynamics and physicochemical aspects of the drug. Based on the mode of drug delivery the physiological characteristics of the GIT and physicochemical characteristic factor the dosage form are designed. The drug development is essential in any case of scientific framework which helps in development of this delivery system. The percent acceptability of oral drug administrations is reported up to the 50 to 60% of dosage forms in spite of difficulty in swallowing tablets and capsule dosage forms [Indurwade et al., (2002)].

Dysphagia is kind of common symptom characterized by problem in difficulty of swallowing especially in pediatric and geriatric patients, by the physiological changes associated with the patients. In view of this problem rapidly dissolving or disintegrating tablets in the oral pediatric and geriatric patients people but are also ideal for active people [Bhushan et al., (2000)]. Presently the population of geriatric patient though is minor, its rate of growth is increased and hence the pharma industry has increasingly aware the need of the drug this group may be considered as a separate group in
pharmaceutical Medicare. The pharmaceutical industry will have significantly impact to the development of oral drug delivery systems. [Bhushan et al., (2000)].

FDT s are dosages, which dissolve fastly in the saliva. FDT are formulated to dissolves in saliva for fast release termed as FD tablets and those contains some superdisintegrants which increases the disintegration of tablets in the mouth cavity, and are named as FD tablets [Prajapati et al., (2009)]. A FDT in more cases, the tablet that dissolve in the mouth without the presence of water. Most of the oral FD drug delivery systems also available in film form contains taste masking agents. This masked active drug content is then swallowing with saliva along to the soluble ingredients and insoluble additives. This is known as melt of tablets in mouth, Porous tablets, dispersible tablets (ODT), quick dissolving tablets [Prajapati et al., (2009)].

1.1 Difficulties Associated with Existing Oral Dosage Forms.

- Swallowing powder and liquids may become difficult in patients who may suffer from tremors.
- There may be gastrointestinal ulceration due to adherence to an esophagus, dysphasia and obstacles.
- Due to the swallowing of solid forms of tablets or capsules dosage forms may produce the difficulty in young adult patients due to incomplete development of nervous system muscular systems.
- The liquid medicaments like, syrups and suspensions stored in multidoses bottles, uniformity of the each dose is difficult.
- The buccal tablets formulation leads irritation to oral cavity of mucosa, due to this reason the patients may refused to take such medications.
- The main factors are cost of products for parenteral preparations which are more costly and discomfort [Panigrahi et al., (2010)].

1.2 Criterion for Fast Dissolving Tablets:

An ideal FDT should have following properties.

- It should be a pleasing mouth feel effect without the need of water for
administration.
• Fast dissolving / disintegrating in mouth in a few seconds.
• It should be acceptable amount of taste masking property.
• After administration of dose it leave minimal residue on the mouth. [Panigrahi et al., (2010)].

1.3 Advantages of FDT:
• Improved compliance/added convenience with superior therapeutic benefit.
• No water and chewing needed with good taste obtained by taste masking.
• It should be formulated to, After administration of dose it leave minimal residue in the mouth.
• Enhanced stability, less sensitivity to different environmentals conditions.
• Suitable for sustained release pattern.[Ghosh et al., (2011)].

1.4 Various Challenges for the development of FDT:
• Bringing the fast disintegration of the tablets.
• Ensure that to avoid tablet the size of tablets.
• Bringing sufficient amount of mechanical strength.
• Ensure minimum residue in the mouth cavity.
• Protection from the environmental conditions like, moisture.
• Good packaging design of tablets. [Bandari et al., (2008)].

1.5 Formulation aspects in developing FDT’s:
• FDT”s are formulated by utilization of different processes, which different in their methodology and different in various properties like, mechanical strength, taste and mouth feeling, swallowability, drug dissolving in saliva, stability and bioavailability [Bandari et al., (2008)].

1.6 Conditions and reasons of using FDT’s:
Type indication:
• Pains, diarrheas, migraine, Anxiety, Insomnia.
• Parkinsons diseases.
• Alzheimers disease.
• Psychosis.
• Hypertension.
• Cholesterol.
• transplantation. [Ghosh et al., (2011)].

1.7 Techniques for the preparation of fast dissolving tablets:

1.7.1 Direct compression technique:
This method involves, the tablets were directly compressed, the drug with excipients directly punched. [Panigrahi et al., (2010)].

1.7.2 Tablet Molding method:
Molded tablets contains ingredients which is soluble in water this leads to rapidly and completely dissolves [Giri et al., (2010)].

1.7.3 Sublimation method: [Giri et al., (2010)].

![Diagram of MDT by Sublimation Techniques]

Figure No-1: The diagram of MDT by Sublimation Techniques.
1.7.4 Lyophilization Method:
The tablets prepared by Lyophilization techniques are very porous in nature. When this tablets contact with the saliva it will quickly disintegrates. [Kaur et al., (2011)].

1.7.5 Spray drying method:
This technique produces fine and porous powder during the process the solvent is evaporated. The technique is used for the production of FDT [Giri et al. (2010)].

Other methods of FDT are
- Mass extrusion.
- Three-dimensional method.
- Printing method.
- Melt granulation method.

1.8 Introduction to Lipids
Cholesterol and triglycerides are the major plasma lipids present in the body which are essential for human health. Cholesterol is synthesized by the liver and is important component of the cell membranes serves as precursors to the bile acid and steroid hormones. Lipids are insoluble in water and they must be transported through blood in specialized complexes, called lipoproteins [Tierona and David Riley., (2009)]

1.8.1 Types of cholesterol:

1. Very low density lipoprotein (VLDL): This cholesterol is composed of 50% to 65% glycerides and 20% to 30% cholesterol and is synthesized by the liver. It is responsible for transporting the triglycerides to adipose and muscular tissue.

2. Low density lipoprotein cholesterol: It is a cholesterol consists of a predominantly cholesterol inner core. It is obtained from the breakdown of the metabolites of VLDL. It is made up of 51% - 58% of cholesterol and 4% - 8% of triglycerides. The important function is to deliver the cholesterol from the liver cells.

3. High density lipoprotein (HDL): This type of cholesterol is a good cholesterol, it protects arterial disease from occurring as it takes away from the cells and back to liver. Once in the liver it is breakdown or excreted from the body in the form of
waste. The HDL is the densest of lipoprotein. Other lipids that play a role in healthy arteries are chylomicrons and triglycerides.

Hyperlipidemia is a disease characterized by increased plasma lipids level may be due to genetic factors (primary) and secondary factors such as diabetes, hypothyroidism, and nephritic syndrome. The daily consumption of food provides required cholesterol and 20%–25% is synthesized by the liver. The remaining is synthesized by the intestine, adrenal glands, reproductive organs and other tissues. Elevated blood levels are harmful and lead to cardiovascular diseases. Particularly the low density lipoproteins cholesterol (LDL), it deposited in the inner wall of large, medium sized arteries such as atherosclerotic plaque. This causes obstruction to the arteries, leads to the hypertension and reduction of oxygenated blood to which is reach to the heart and leads to increase the risk of coronary heart diseases, myocardium infarctions and cerebral arterials disease. The liver of an individual with average frame and weight synthesizes about 1000 mg of cholesterol daily. The total cholesterol content of the body is approximately 35 grams. It is transferred by the bile into the intestinal tract. About 50% of excreted cholesterol is reabsorbed by the digestive system and pumped back into circulation. This cholesterol recycling is continuous in nature [Tierona and David Riley, (2009)].

1.8.2 Causes of hyperlipidemia:

Hyperlipidemia is mainly due to genetic and environmental factors, including:

1) Presence of diseases such as diabetes, hypertension, hypertriglyceridemia, kidney and liver related diseases.
2) Family history to developing CHD or CVA early in their life (under 55 for brother and father and under 65 years of age for mother and sister).
3) Gender: Men have more risk to developing hyperlipidemia compared to women.
4) Age: A person becomes older, so there may be chance for developing atherosclerosis.
5) Many foods like eggs, butter, liver, kidneys, and certain sea foods contain cholesterol, and other foods, like red meat, many cheeses, creamy cakes, ice
cream, sausages and hot dogs have high contents of saturated fats and may affect to outcome of cholesterol blood concentration.

6) Sedentary lifestyle: It has been shown that non-vigorous physical activity leads to reduce LDL and elevate HDL blood levels. The bad habits such as smoking and over bodyweight are also responsible for hyperlipidaemia.

1.8.4 Major risks of Hyperlipidaemias:

1. Atherosclerosis:

It is a disorder, occurs when the cholesterol, fat and calcium deposits in the arterial linings form multiple plaques. A plaque normally consists of three components Atheroma it is a fatty, soft, yellowish nodular mass deposit in the centre of a larger plaque that is consists of macrophages, which are the cells that play a role in immunity. A layer of cholesterol crystals. Calcified outer layer. Atherosclerosis is leads to cardiovascular disease.

2. Coronary Artery Disease:

It is a condition which arteries are narrowing leads to less supply the blood to myocardium, and results in limiting blood flow and insufficient amounts of oxygen to meet the needs of the heart. The narrowing may progress to the extent that the heart muscle would sustain damage due to lack of blood supply.

3. Myocardial Infarction:

It is a condition, when blood and oxygen supplies are partially or completely blocked from flowing in one or more cardiac arteries, leads to damage or death of heart cells. The blockage is by formation of a clot in the artery. This condition is known as heart attack.

3. Angina Pectoris:

It is termed as angina, this condition is not an disease. This is characterized by chest pain, discomfort or a squeezing pressure. The pain may be felt in the shoulders, arms, neck and back. Angina is a condition occurs as a result of reduction or lack of blood supply to a part or the entire heart muscle and impairment of waste removal. Poor blood circulation
is usually due to CHD when partial or complete obstruction of the coronary arteries is present. Angina attacks may be spasm of the arteries. Angina may be a symptom of coronary micro vascular disease (MVD), a condition that affects the heart’s smallest arteries.

4. Stroke (CVA):

This condition affects, when blood circulation of the brain is blocked. The blood supply which carries oxygen, glucose, and other nutrients is disrupted leads to brain cells die and become dysfunctional. Usually the strokes occur due to blockage of artery by a blood clot that breaks loose in a small vessel within the brain.

1.8.5 Treatment of Hyperlipidaemia:

Since lifestyle plays an important role in contributing to hyperlipidaemias, it more important to realize that TLC should be instituted and followed. The lowering of blood cholesterol level cannot be achieved alone, use of drugs becomes necessary.

1.8.5.1 Treatments:

1. Therapeutic Lifestyle Changes:

Diet alteration and weight reduction should be tried as initial important treatment, especially in mild cases of hyperlipidaemias, in persons without CHD less than 2 risk factors. It must be kept in mind that when dieting, cholesterol intake is reduced. At the same time, production of cholesterol, especially by the liver, increases. It is strongly recommended that the intake must be restricted to 25% to 35% of intake of energy and saturated fatty acids make up < 7% of intake of energy, and intake of cholesterol should be < 200 mg daily. The plant sterol esters and soluble fibre is most advisable. Healthy diet can result in 10% to 15% reduction of the cholesterol blood level.

2. Drug Therapy:

High, Low DL, in presence of some risk factors, and recording of Coronary Heart Diseases should qualify initiating drug therapy with TLC. Mono therapy has showed to be effectiveness in treatment of hyperlipidemia and combination therapy of treatment
may be required for this approach. Current lipid-lowering drugs include statins, ezetimibe, fabric acid derivative, and sterols [Tierona and David Riley., (2009)].

1.9 Statin are employed in the treatment of Hyperlipidaemia:
Statins are the most common medications used in the treatment of hyperlipidaemias. Last year more than 20 million Americans were taking statins. They are also referred to as HMG-CoA Reductase Inhibitors because of their mechanism of action. They are well tolerated and effective in lowering LDL. Additionally, they have high level of patients compliance due to their tolerable adverse effects.

1.9.1 Adverse Effects of Statins:
   1) Rhabdomyolysis
   2) Myalgia
   3) Muscle cramps.

1.9.2 Statins in Current Use:
The statins in use are pravastatin lovastatin, simvastatin, fluvastin, atorvastatin, pitavastatin and rosuvastatin. Comparison of efficacy of these drugs concluded that atorvastatin in reduction of LDL of 42%. Lovastatin and simvastatin are reductions of 36%. The triglyceride reduction by 19% atorvastatin, simvastatin 13%, lovastatin 12% and HDL serum level increased by 5% to 6% with all statins.

Lovastatin:
The lovastatin occurs naturally and it is found in food such as oyster mushrooms, the FDA was approved the lovastatin first. After the oral administration presence of Food enhance the absorption rate. The side effects are abdominal pain, cramps, and dyspepsia, are usually. The dose of lovastatin different from one person to another person’s and should determine the response of the patient and requirement of the patients. The normal maintenance dosage is 10 to 80 mg/ day given to the patients in a divided dose or single dosage.
Pravastatin:
The normal maintenance dose is 10 to 40 mg/day. The drug should be taken with food, meal and it does not appears to affect of its activity. Pravastatin side effects include abdominal cramp, nausea, vomiting’$s$, diarrheas, flatulences, headache.

Simvastatin:
The due to increased risk of myopathy the normal maintenance dose is 80 mg/day, usually during the first 20 month. The side effects include abdominal cramp, nausea, vomiting’$s$, diarrheas, flatulence’$s$, headache. Muscle weakness and myalgia was are rarely reported. The 20 mg/ day dosage is. usual initial dose for adult. A dose of 20 mg daily is initiated, this may be increased at intervals of not ≤ 4 weeks until a maximum dose of 80 mg is reached.
Figure No-2: The figure of cholesterol transport in the tissues, with sites of action of the main drugs affecting lipoprotein metabolism [Rang et al., (2003)].
**Fluvastatin:**
The recommended dose of fluvastatins posesses a low incidence of side effect that are normally tolerated. The most common ones are abdominal discomfort, headache, back pain and rash [Sadik et al., (2013)].

**Statins:**
The statins were isolated from the mold of, *Penicillium citrum* and is identified as inhibitors of cholesterol biosynthesis in the year 1976, Discovered by Endo and colleagues. (Rang et al., (2003)).

**1.10 Studies on Solubility Improvement:**
The important property of a dosage forms, to deliver of the potent ingredients to its specific sites at definite rate and amount sufficient to for the desired pharmacological action.

**1.10.1 Approach used for increasing the dissolution rate of insoluble drugs:**
The three approaches which is overcoming the problems of bioavailability and insoluble drugs.

**1.10.1.1 The Pharmaceuticals Approaches:**
This involves the different modification of formulations, without changing the chemical structures of manufacturing, process or physicochemical characters of drugs.

**1.10.1.2 The Pharmacokinetic Approach:**
In which the pharmacokinetics of drugs is altered by modifying its chemical structure of the drug.

**1.10.1.3 The Biological Approaches:**
The approach of chemical structure modification has a number of draw backs like very expensive and time consuming, require repetition of studies and a long time is required for regulatory approval. The aim of drug is to enhancement of rate of dissolution, for that
optimizing the formulations, manufacturing process or physicochemical properties of drugs.

1.10.2 The different Methods are as follows:

- **Micronization method:**
  This process involves reductions of the sizes of the solid drugs to 1 to 10 micron size is usually by the methods of air attritions. Example the drugs of dosage forms whose bioavailability is increased by the process of micronization includes the griessofulvin and several sulfa drugs.

- **Use of surfactants method:**
  In this method the surface active agents are enhance the rate of dissolution is the primary by wetting, promoting and penetrations into the dissolution fluid to the solid particles. They were normally used in the concentration below their Critical Micellaras Concentration value or above the CMC. The drug entrance into the micelles structure fail to partition into the medium of dissolution. The nonionic surface active agents like polysorbate are widely used in this method. Example the drugs of dosage forms whose bioavailability is increased by the process of surface-active includes the steroid like spironolactones.

- **Use of salt Forms:**
  In this method the salts forms have increases the solubility and rate of disso in comparing to the pure drug. The metal salts of acidic dosage forms like penicillin and strong acid salt of basic drug example atropine are more water soluble than the pure drug of same.

- **Alterations of the pH of Drug in the Micro environments:**
  This can be achieved by two way, normally in situ salts formations and the additions of buffer to the formulation. Examples. Buffered aspirin tablet.
• **Use of the metastable polymorph:**
  This method a metastable polymorph is high soluble compare to the stable polymorphs of a drug and which exhibit polymorphisms. Example, The B form of chloramphenicol is highly soluble compared to the A and C forms chloramphenicol drugs.

• **Solute to Solvents complexation:**
  In this method the solvates of drugs with organic solvents have increases the aqueous solubility compared to their respective hydrates of pure drug. The much increased solubility can be attained by the method of freeze drying such as, solutes in solution with an organic solvent with which it is called as solvates. Example 1:2 ratio griesofulvin to benzene solvates complexations.

• **Solvents deposition method:**
  In this method, low soluble drugs such as nifedipine is dissolve in the organic solvents like alcohols and deposits in the inserts, hydrophilic, solids matrixs such as microcrystalline celluloses by the evaporation of solvents.

• **Selective adsorptions on in soluble carrier:**
  A highly actives adsorbents such as inorganic clay such as bentonite will be increases the rate of dissolution of poorly soluble drug such as griesofulvin, Indometacin and prednisolon by maintaining their conc. gradients at the maximum levels. 2 reasons that suggests for rapids releases of drug from the weak physically bondings between the adsorbates, adsorbents, hydration and swelling of the clays in the aqueous medias.

• **Solid solution:**
  In this method the particle sizes of a drugs can be reduced to sub microns level by the use of solid solutions, use of eutectic mixture and use of solid dispersion technique.
In all these cases, the solutes is frequently a low water soluble drugs acting as the guest and the solvents is highly water soluble compound acting as a host or carrier [Leuner et al., (2000), Brahankar et al., (1995)].

1.11 Cyclodextrins:

CD comprises a family of water soluble, non-reducing, oligosaccharide which are having the abilities to forms molecules inclusions with hydrophobics drug have low AQS parameters. The CD molecules are having the versatility nature and have a hydrophobic cavities of sizes suitable molecules, having enough space to incorporate the lipophilic drug as guest which fits to the outsides of the host molecule is hydrophilics cavity. Thus the molecular encapsulation of the drug has great improve of aqueous solubility and rate of dissolution [Gerold et al., (2002)]. CD is a groups of structurally related saccharide which formed by the enzymatic cyclizations of starch by a group of amylase enzyme called as glycoyl transferase. In the pharmaceutical industries, CD have been used as a agents which complexes and increases AQS of low solublity drugs. By this complexation increases the stability and bioavailability of drugs.

In additions, CD can be used to reduces or prevents gastrointestinal irritations, reduces or eliminates unpleasant smell, it prevents drug to drug interactions powders[Loftsson et al., (1996), Wade et al., (1994)]. They were used in formulations of oral and topically applied drug to enhance their stabilities of low solubility drugs, bioavailability and to reduces the side effects. [Szeijtli., (2004)].
1.11.1 The Encapsulation with CD:

The beta Cyclodextrins and gamma Cyclodextrins they have the several of their derivatives which are unique abilities to form the moleculars inclusions with hydrophobic drug have low water AQS. These CD molecule contain a hydrophobic cavities of sizes suitable with accommodates the lipophilic drug as guest molecule to fit the outer side of the host molecule which is relatively hydrophilic in nature. Thus molecular encapsulation of drug has great improved AQS and disso rate. Amongs the possibilities, the preparations of inclusions complex with cyclodextrins is of particularly interest [Brewster and Loftsson ., (2007)].

1.12 Methods of preparation of inclusion complex:

- Physical mixtur method.
- Kneadings method.
- Microwave irradiation methods.
- Spray drying method.
- Freeze drying method.
• Solid dispersion method.
• Neutralization method.
• Co-evaporation method.
• Co-centrifugation method.

1.13 Stability study:
The stability is depends upon the environmental factors, ingredients used and the nature of the container can be affect the stability of the drug and its doses forms and it also affects the powder formulations.
The loss of potency usually occurs from a chemical change, the most common reactions is by the hydrolysis, oxidations and reductions takes place. Potency is determined by the means of an assay procedure that will differentiate between the intact drug and its degradation product. Accelerating the decomposing process and to extrapolating the result to normal storage conditions may make to prediction of the life of the product. Acceleration of the chemical decomposition is achieved by raising the temperature of the preparations.
The principles of chemical kinetics to the results of accelerated storage test carried out at three elevated temperatures conditions, enable prediction to be made for the effective life of the preparation, at normal temperature range. Plotting the graph of appropriate function of concentration against the time and from the graph, obtaining a linear relationship curve, which determines the rate of the reaction for the process of decomposition.
The reaction velocity of the constant k, for the decomposition at each of the elevated temperature, can calculate by the slope of the line. The most satisfactory method for expressing the influence of temperature on reaction velocity is quantitative relation proposed by Arrhenius.

\[ K = Ae^{-\frac{Ea}{RT}} \]

K = Specific rates of degradation.
R = Gas Constants.
\[ T = \text{Absolute temperatur.} \]
\[ A = \text{Frequency factors.} \]
\[ \text{Ea} = \text{Activation of Energy.} \]

The Arrhenius equation is then employed to determine the „K” value for decomposition at the room temperature. This is obtained from the graph, linear plot of the logarithm of „k” value against reciprocal of absolute temperature, which is then extrapolated to the room temperature. The value of K at 25° c may be then substituted in the appropriate rate of the equation and an estimate obtained of time during which the product will maintain the required quality (shelf-life).

Below table indicates maximum time and minimum time at which potency is at least 90% of the label claims.

**Table No-1: Stability Requirement for Maintenance of Shelf-Life.**

<table>
<thead>
<tr>
<th>Temperature °C</th>
<th>Maximum time</th>
<th>Minimum time</th>
</tr>
</thead>
<tbody>
<tr>
<td>37°C</td>
<td>12 months</td>
<td>6.4 months.</td>
</tr>
<tr>
<td>45° C</td>
<td>8.3 months</td>
<td>2.9 months.</td>
</tr>
<tr>
<td>60° C</td>
<td>4.1 months</td>
<td>3 weeks.</td>
</tr>
<tr>
<td>85° C</td>
<td>6 weeks</td>
<td>2.5 days</td>
</tr>
</tbody>
</table>

If the assay is over 90% of the original potency at the minimum time (with activation energy 20 K cals/mol.) at the respective temperature ranges. In all probability the assays will be over 90% after two years at a room temperature. If the assay remain over 90% at the time shown, (with activation energy 10 K cals/mol.) it is certain that a potency of over 90% is maintained after the 2 years at room temperatures. [Lachaman et al., (1987)].
1.14 Methods for detections of inclusion complexes, formations and determination of complexes stability constant:
The most interesting properties of CD is form complex with wide varieties of guests molecules encapsulations with host molecule. The molecular encapsulations may be occurs both in liquid and solid states. In the solutions there is an equilibrium occurs between complexes and non complexes guest molecule. In solid states of guest molecule can be entrapped within their cavity or aggregated with outside of the CDs molecules. Upon inclusion complexes with in the CDs cavity a guest molecules experiences change in its physicochemical properties of the molecule.

1.14.1 Detections of inclusion complexes in the solutions state:
Detections of complexes in the solutions state can be done by spectroscopic methods like
1. UV-visible spectrophotometers
2. Florescence spectroscopy
3. Circular dichroism
3. ESR
4. NMR spectroscopy methods

The $^1$H-NMR and $^{13}$C-NMR spectroscopic studies can used to determined the directions of penetrations of the guest molecule into the host CDs cavities. The other methods used for this study like
1. Polarography
2. Conductivity measurements
3. Microcalorimetry
4. Solubility methods
From the all above methods, the phase solubility technique is one of the most widely used methods.
1.14.2 Phase solubility techniques:

It is the method for to study of complexes is termed as phase solubility study, described by the scientists called Higuchi and Connor, which study the complexing agents effects. The phase solubility figures are classified into A and B type of curve.

**The different type of curves in phase solubility techniques are**

1. A type curves
2. B type curves
3. AB1 type curves
4. AS type curves
5. ABS type curves
6. AL type curves
7. BS type curves
8. AP type curves and AL type curves.

**Figure No-3: Theoretical phase solubility diagram.**

In case of a 1:1 stoichiometric complexes, using the following equations we can determined the equilibrium constant, $K$ from the graph to the slope of the linear portion of the curves.

$$K_{a,b} = \frac{\text{slope}}{S_0 \ (1-\text{slope})}$$
\( S_0 \) is intrinsic solubility of the drugs.

Equilibrium binding of drugs and CDs to form a 1:1 complex can be represented as:

\[
\text{Drug} + \text{CD} \leftrightarrow \text{Drug-CD Complex}
\]

Since equilibrium binding is usually established with half-lives of much less than one second, the kinetic of dissociation of drug with CDs complexes are generally expected to much faster than many physiological processes.

### 1.14.3 Detections of inclusion complexes in solid states:

Detections of the complexes in solid states can be done by powder X-rays diffractometry, X-ray structure analysis, thermo analyses, chromatography, paper chromatography, IR spectroscopy, Scanning electron microscopy and dissolution study methods.

### 1.15 Application of \( \beta \)-cyclodextrin inclusion complexes:

CDs used in drug formulation either for Complexations or as additives. Complexation with CD has the following applications:

- Improvements of physical and chemical stabilities of the drugs.
- Enhances the Bioavailability of poorly soluble drugs.
- In liquid drug formulations (injections, ophthalmic and nasal preparations) [Loftsson and Duchene., (2007)].