IJPSR (2016), Vol. 7, Issue 6 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 16 December, 2015; received in revised form, 26 March, 2016; accepted, 03 April, 2016; published 01 June, 2016

A REVIEW ON PHARMACEUTICAL PREFORMULATION STUDIES IN FORMULATION AND DEVELOPMENT OF NEW DRUG MOLECULES

Gita Chaurasia

Department of Pharmaceutics, Siddhant College of pharmacy, Sudumbare, Pune, Maharashtra, India

Key words:

Preformulation, Stability, Physico-Chemical properties, Preformulation evaluation, Parenteral.

Correspondence to Author:
Gita Chaurasia

Assistant Professor,
Department of Pharmaceutics,
Siddhant College of pharmacy,
Chakan-talegaon road, tal.-maval
Sudumbare, Pune, Maharashtra, India
412109

E mail: gitagc@yahoo.co.in

ABSTRACT: Preformulation is a group of studies that focus on the physicochemical properties of a new drug candidate that could affect the drug performance and the development of a dosage form. This could provide important information for formulation design or support the need for molecular modification. Every drug has intrinsic chemical and physical properties which has been consider before development of pharmaceutical formulation. This property provides the framework for drugs combination with pharmaceutical ingredients in the fabrication of dosage form. Objective of preformulation study is to develop the elegant, stable, effective and safe dosage form by establishing kinetic rate profile, compatibility with the other ingredients and establish Physico-chemical parameter of new drug substances. Among these properties, drug solubility, partition coefficient, dissolution rate, polymorphic forms and stability are plays important role in preformulation study. Polymorphism having crystal and amorphous forms shows different chemical physical and therapeutic description of the drug molecule. This article explains some properties and techniques for preformulation evaluation parameters of drug.

INTRODUCTION: Preformulation evolved in the late 1950s and early 1960s as a result of a shift in emphasis in industrial pharmaceutical product development. It was improvement in analytical methods that spurred the first programs that might bear the name "preformulation". The overall objective of preformulation testing is to generate information useful to the formulator in developing stable and bioavailable dosage forms which can be mass-produced.

QUICK RESPONSE CODE

DOI:
10.13040/IJPSR.0975-8232.7(6).2313-20

Article can be accessed online on:
www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.7 (6).2313-20

During the early development of a new drug substance, the synthetic chemist, alone or in co-operation with specialists in other disciplines including preformulation, may record some data which can be appropriately considered as preformulation data.

Before starting the preformulation studies we should know the properties of the drug, potency relative to the competitive products and the dosage form, literature search providing stability and decay data, the proposed route of drug administration, literature search regarding the formulation approaches, bioavailability and pharmacokinetics of chemically related drugs. It also includes preliminary investigations and molecular optimization by the drug should be tested to

determine the magnitude of each Suspected problem area (Step I), if a deficiency is detected, a molecular modification should be done(Step II). To overcome this deficiency molecular modification is done be salts, prodrugs, solvates, polymorphs or even new analogues. The dissolution rate of a salt form of a drug is generally quite different from that of the parent compound. Sodium and potassium salts of weak organic acids and hydrochloride salts of weak organic bases dissolve much more readily than do the, respective free acids or bases. For Example Ephedrine base is very poorly water soluble molecules that characterized by low solubility and dissolution rates. So, it is modified in the form of the salt Ephedrine HCL that is ionized and offer higher water solubility and dissolution rate. Prodrug formation is the formation of synthetic derivatives of the drug (e.g. esters or amides) that liberate the active drug *in-vivo*. Prodrug may or may not have a pharmacological activity.

The active drug is released by acidic medium, enzyme action, etc. Prodrug formation may increase the absorption rate due to its lipophilicity (passive) or its water solubility (active). Prodrug formation may increase the duration of action. Prodrug formation may improve the drug stability, solubility, crystallinity, taste, odor and reduced pain on injection. For example Erythromycin base has a bitter taste and is rapidly hydrolyzed in stomach to inactive products. Erythromycin Estolate (Prodrug of erythromycin) is inactive and tasteless. It has 4 times absorption rate. It is hydrolyzed by the acid in stomach to liberate the free base which is active. [1] **Table 1** describes some evaluation parameters used in preformulation of drug development.

TABLE 1: EVALUATION PARAMETERS USED IN PREFORMULATION OF DRUG DEVELOPMENT

S.No	Parameters	Evaluation parameters
1.	Stability	Temperature, Light, humidity
	Solid State	Solvent, Ph
	Solution	
2.	Solid State Compatibility	TLC and DRS Analysis
3.	Physico-chemical Properties Color, odor, particle size, shape crystallinity	Molecular Structure and Weight, melting point
4.	Thermal Analysis Profile Solubility	DTA, DSC,TGA
	Water and other solvent, pH	Salt forms, co-solvent, Complexation, pro-drug
5.	Absorbance Spectra	UV, IR
6.	Other properties Hygroscopicity	Potential Bulk characterization Volatility, optical activity, solvate formation Crystallinity and polymorphism
7.	Physico-mechanical Properties Bulk and	Tapped density, compressibility Photomicrograph
8.	In Vitro Availability Properties Rat Everted Gut Technique	Dissolution and analysis of Drug Crystal, pallets
9.	Other Studies Plasma Protein-Binding, Ionization Constant	Effect of Compatible Excipients on dissolution, Kinetic Studies of Solution Degradation, Use of Radio-labeled Drug

Physicochemical parameters: [2]

1. Organoleptic properties:

2. Bulk characterization studies:

a) Crystallinity and polymorphism

b) Hygroscopicity

c) Fine particle characterization

d) Bulk density e) Powder flow properties

f) Compression propertiesg) Physical description

3. Solubility analysis:

a) Intrinsic solubility determination

b) PKa determination

c) Partition coefficient

d) Dissolution studiese) Common ion effect

4. Stability analysis:

a) In toxicology formulations

b) Solution stability

c) Solid state stability

1. Organoleptic properties:

Color: It should be Unappealing to the eye and determined by either instrumental methods or visible method that varies from batch to batch. Record of early batches and establishing "specs" is very useful for later production. Coating of body in variable color can be done if found undesirable.

Odor and taste:
For unpalatable drug use of less soluble chemical form or suppress it by flavors, excipients, coating etc. Drug substances which irritating to skin should be handle with precautions. Flavors, dyes, excipients used will affect stability and bioavailability. Color may be off-white, cream yellow, tan, shiny. Odor may be pungent, sulfurous, fruity, aromatic and odorless. Taste may be acidic, bitter, bland, intense, sweet and tasteless.

2. Bulk characterization studies:
It is needed to identify all the solid forms that may exist as a consequence of the synthetic stage such as the presence of polymorphs. Bulks properties such as particle size, bulk density, surface morphology may be changed during the development process and to avoid mislead predictions of solubility and stability which depends on a particular crystalline form. Bulk characterization testing includes:

a) Crystallinity and polymorphism:
The structure of a solid compound refers as crystallinity and these structures disappear in the liquid and vapor states. It can be classifies as Internal structures (cubic, tetragonal, hexagonal, rhombic, etc.), Solid habits (platy, needle, tabular, prismatic, bladed, etc.), Changing the internal structures alter the crystal habits, Changing the chemical form (e.g. salt formation) alter both the internal structure and crystal habit. Different polymorphs are obtained by crystallization from different solvents and by solidification after melting. When the incorporated solvent is water, it is called "hydrates". The compound not containing any water within its crystal structure is called as "anhydrous".

Atoms in crystalline matter are arranged in regular and repeating patterns in three dimensions. e.g. metal and mineral and atoms or molecules randomly placed without a regular atomic arrangement in amorphous solids. Polymorphism is the ability of the compound to crystallize as more than one distinct crystalline species with different internal lattice and different crystal forms (at different free energy states) of the same compounds. They have different physicochemical properties (melting point, density, vapor pressure, X-ray, color, crystal shape, hardness, solubility, dissolution rate and bioavailability). During preformulation, it is important to identify the polymorph that is stable at room temperature. For examples: Chloromphenicol exist in A, B& C forms, of these B form is more stable and most preferable. Riboflavin has I, II& III forms, and the III form shows 20 times more water solubility than form I. Enantiotropic polymorphs can be inter converted below the melting point of either polymorph and the conversion is reversible at a define temperature. E.g. sulfur.

In Monotropicpolymorphs the transition takes place in one direction (irreversible). E.g. glyceryl stearate and diamond graphite. Stable polymorph has low free energy, low solubility and high melting point. Metastable polymorph is less stable with higher solubility and bioavailability and lower melting point.[3] Crystals and polymorphs are characterized by Microscopy, Thermal analysis and X-ray diffraction method. Significances of identification of crystal shape and internal structure can influence by Solubility and stability-For example: Chloramphenicol palmitate exists in 3 crystalline polymorphic forms (A, B and C) and an amorphous form (D). Increasing the concentration of the form B led to increase the serum level due to its higher water solubility. Melting point-For example: Cacao butter as an oily base for suppositories exists in four polymorphic forms (α, β-prime, γ and β-stable). Only the β-stable form can be used as a suppository base due to its higher melting point. Density and Crystal shape influences the flow properties of powders. Tablet hardness influence the compression properties and grinding processes.

Pharmaceutical applications of polymorphism:
In suspension phase transformation from unstable form to more stable polymorph can cause changes in crystal size and caking. e.g. Oxyclozanide (anthlemintic). In creamcrystal growth as a result of phase transformation can cause grittiness. In suppositories changes in polymorphic forms could cause product with different and unacceptable melting characteristic (failure to melt after administration or premature melting during storage). E.g. theobroma oil "suppositories base". It leads characterization of solids that involves varification of solid in expected chemical

compound, characterization the internal structure, describing the habit of crystal; determine how many polymorphs may exist for the compound and stability, screening for the presence of an amorphous form etc.

a) Hygroscopicity:

Many drug substances exhibit a tendency to absorb moisture. The amount of moisture adsorbed by a fixed weight of anhydrous sample in equilibrium with the moisture of the air at a given temperature. These are classified as Deliquescent (a substance which absorb sufficient moisture from the atmosphere to dissolve itself at higher extreme), Efflorescent (a substance which loses water to form a lower hydrate or become anhydrous at lower level) and Hygroscopic (a substance that exist in a dynamic equilibrium with water). This process depends on the relative humidity of the surroundings. It is characterized by Karl fisher, gravimetric, TGA, or Gas chromatography methods. It is significances as changes in moisture content that affects stability, flow ability, compatibility, etc.

b) Fine particle characterization:

Certain physical and chemical properties of drug substances are affected by the particle size distribution, including drug dissolution rate, bioavailability, content uniformity, taste, texture color, and stability. In addition, properties such as flow characteristics and sedimentation rates, among others, are also important factors related to particle size. It is essential to establish as early as possible how the particle size of the drug substance may affect formulation and product efficacy. Methods of evaluation of particle size and distribution includes light microscope with a calibrated grid, Sedimentation techniques, Stream scanning, Coulter counter and Surface area determination by BET nitrogen adsorption method.

c) Bulk density:

Knowledge of the true and bulk densities of the drug substance is very useful in forming some idea as to the size of the final dosage form. Obviously, this parameter is very critical for drugs of low potency, which may constitute the bulk of the final granulation or table. Bulk density of a compound varies substantially with the method of crystallization, milling or formulation once a density problem is identified it is often easily corrected by milling slugging or formulation.It can affect powder flow properties.It affects the size of high dose capsule product or the homogeneity of a low dose formulation in which there are large differences in drug and excipients densities.

d) Powder flow properties:

The flow properties of powders are critical for an efficient tablet operation.During the pre-formulation evaluation of the drug substance, therefore, its flow ability characteristic should be studied, especially when the anticipated dose of the drug is large.Powders may be free flowing or cohesive (non free flowing).Flow properties are affected by changes in particle size, density, shape, electrostatic charges, and adsorbed moisture. It is characterized by Carr's index and Hausner ratio, Angle of repose, rheology and thixotropy etc.[4]

e) Compression properties:

The compression properties (elasticity, plasticity, fragment ability and punch filming propensity) for small quantities of a new drug candidate can be established. This property is used in proper selection of the formulation ingredients.

f) Physical description:

It is possible to observe on the bases of size, shape, appearance and determined instrumentally or visually.

3. Solubility analysis:

One important goal of the pre-formulation effort is to devise a method for making solutions of the drug. A drug must possess some aqueous solubility for therapeutic efficacy. In order for a drug to enter the systemic circulation to exert a therapeutic effect, it must first be in solution. Relatively insoluble compounds often exhibit incomplete absorption. When a solute dissolves, the substance's inter molecular forces of attraction must be overcome by forces of attraction between solute and solvent molecules.

This involves breaking the solute-solute forces and the solvent-solvent forces to achieve the solute-solvent attraction. It focuses on drug-solvent interactions that could occur during the delivery of

a drug candidate. For example, orally administered drug should be examined for solubility in simulated gastric media. We need to perform solubility analysis of a new drug to provide a basis for later formulation work and can affect drug performance. Drugs with an aqueous solubility less than 1% (10 mg/ml) will suffer from bio absorption problems. Factors affecting the solubility of a drug are temperature, Chemical and physical properties of both the solute and the solvent, Pressure, acidity or basicity of the solution, state of subdivision of the solute and solvent, physical agitation applied to the solution during the dissolving process etc. Methods of Solubility analysis include: Solubility determination, pKa determination, Partition coefficient, Dissolution behavior, Common ion effect, Membrane permeability. Methods to improve drug solubility are chemical modification of the drug into salt or ester forms, through selection of a different solubilizing agent, use of co-solvents or other techniques such as micronization or solid dispersion and adjustment of the pH of the solvent in which the drug is to bedissolved.[5]

a) Intrinsic Solubility determination:

Steps: I All factors that affect the solubility and dissolution should be defined.

Steps: II An excess amount of the drug is dispersed in the medium and agitate at constant temperature.

Steps: III Withdraw Samples of the slurry as a function of time.

Steps: IV ClarifyAmpoules by filtration or centrifugation.

Steps: V Assay the clear samples for its drug content to establish a plateauconcentration and analyze using UV, HPLC, and GC…etc.

b) pKa determination: The interrelationship of the dissociation constant, lipid solubility and pH at the absorption site and absorption characteristics of various drugs are the basis of the pH-partition theory. Dissociation constant or pKa is usually determined by potentiometric titration. The majority of drugs today are weak organic acids or bases. Knowledge of their individual ionization or dissociation characteristics is important, because their absorption is governed to a large extent by their degrees of ionization as they are presented to the membrane barriers. The degree of a drug's ionization depends both on the pH of the solution in which it is presented to the biologic membrane and on the pKa, or dissociation constant, of the drug (whether an acid or base).The concept of pKa is derived from the Henderson-Hasselbalch equation:

For acidic compounds pH=pKa + log (ionized drug/ unionized drug)

For basic compounds pH= Pkw - pKb + log (unionized drug/ionized drug)

The ideal pH of parenteral products is pH 7.4. If pH is above 9, tissue necrosis may result while below 3, pain and phlebitis in tissue can occur. Buffers are included in injections to maintain the pH of parenteral products e.g., citrates, phosphates etc. [6]

Significances:

1. Provided that the intrinsic solubility and pKa are known, the solubility at any pH can be predicted.

2. Henderson equations can facilitate the selection of suitable salt forming compounds and predict salts' solubility.

3. Determination of the ratio of the ionized to the unionized form of a drug molecule. This is useful to predict which form will predominate at different Physiologic pH. Mostly, the unionized form of the drug is the one absorbed. Consequently, acidic drugs will be absorbed in the acidic media of the stomach and vice versa.

Partition coefficient- The oil/water partition coefficient is a measure of a molecule's lipophilic characters that is, its preference for the hydrophilic or lipophilic phase. The partition coefficient should be considered in developing a drug substance into a dosage form. If a solute is added to a mixture of two immiscible liquids, it will distribute between the two phases and reach equilibrium at a constant

temperature. The distribution of the solute (un-aggregated & un-dissociated) between the two immiscible layers can be described as follows: it is the ratio of the unionized drug distributed between the organic (upper phase) and aqueous (lower) phases at equilibrium.

Determination of partition coefficient:

Shake flask method: the drug dissolved in one solvent is shaken with the other partitioning solvent for 30 min. The mixture allowed standing for 5 min. The aqueous solution is centrifuged and then assayed for drug content. It has a number of applications such as:

1. Used in Solubility determination of both in aqueous and mixed solvents.

2. It is applied to a homologous drug series for structure activity relationships indrug absorption *in-vivo*.

3. Partition chromatography can be helpful for column and stationary phase selection (HPLC), choice of plates for TLC and choice of mobile phases (eluents).

4. This information can be effectively used in the extraction of crude drugs.

5. Recovery of antibiotics from fermentation broths and recovery of biotechnology-derived drugs from bacterial cultures.

6. Extraction of drugs from biologic fluids for therapeutic drug monitoring.

7. Absorption of drugs from dosage forms (ointments, supp, TDDS) and study of the distribution of flavoring oil between oil and water phases of emulsions.

d) Dissolution studies: The speed or rate at which drug substance dissolves in a medium is called dissolution rate. Dissolution rate data when considered along with data on a drug's solubility, dissociation constant and partition coefficient can provide an indication of the drug's absorption potential following administration. The dissolution rate of the drug in which the surface area is constant during dissolution is described by Noyes Whitney equation as follows-

$$\frac{dc}{dt} = \frac{D\,A\,(Cs-C)}{h\,V}$$

D: diffusion coefficient
h: thickness of the diffusion layer at solid liquid interface.
A: the surface area of the drug in contact with the dissolution medium.
V: volume of media.
Cs: saturated solubility of the drug in the dissolution medium at exp. Temp.
C: the concentration of the drug at time t.

The equation reveals that the dissolution rate of a drug may be increased by increasing the surface area (reducing the particle size) of the drug and by increasing the solubility of the drug in the diffusion layer.[7]

Significances:

c) Taking into consideration the intrinsic solubility data, dissolution studies can identify potential bioavailability problems. For example: dissolution of solvates and polymorphs can have an impact on the bioavailability and drug delivery.

d) It is useful in predicting probable absorption problems due to dissolution rate. In particulate dissolution, a weighed, amount of powdered sample is added to the dissolution medium in a constant agitation system.

e) This method is frequently used to study the influence of particle size, surface area, and excipients upon the active agent.

f) Occasionally, an inverse relationship of particle size to dissolution is noted due to the surface properties of the drug.

e) Common ion effect- The addition of a common ion reduces the solubility of the slightly soluble electrolyte. This salting out(drug precipitation) results from the removal of solvent molecules from the surface of the electrolyte by the hydration of the common ion. Salting in larger anions (hydro tropes) e.g. benzoates, salicylates can open the water molecules allowing an increase in solubility of poorly-water soluble drugs.

Example hydrochloride salts often exhibit lower solubility in gastric juice due to the abundance of the chloride ions. To explore a common ion interaction, the dissolution rate of a hydrochloride salt should be compared in different media: Water and 1.2% w/v NaCl, 0.05 M HCl and 0.9% w/v NaCl in 0.05 M HCl. It is useful in the choice of a suitable salt form for the proper dissolution and accordingly enhanced absorption. Factors affecting degradation rates are temperature, Effect of pH and others such as ionic strength, co-solvent, presence and absence of O_2, presence of antioxidants and presence of chelating agent. The primary goal of this approach is to identify the storage conditions and additives to form a stable solution preparation. For example: Antioxidants (Sod. sulphite, Sod. Thiosulphate, ascorbic acid, BHA and BHT), Chelating agents (EDTA), Replacement of O_2 by CO_2 or N_2, Use of co-solvents (propylene glycol, ethanol) to replace part of the aqueous vehicle for enhancing solubility, stability and Storage at low temperatures.

4. Stability analysis:

a) In toxicology formulations:

These studies are advisable to evaluate samples of toxicology preparations for stability and potential homogeneity problems. Usually a drug is administered to the animals in their feed, or by oral gavages of a solution or suspension of drug in an aqueous vehicle. Water, vitamins, minerals (metal ions), enzymes and moisture levels present in feed, which can severely reduce the shelf life of a drug and decrease stability. Solution and suspension toxicological preparation should be checked for ease of manufacture and stored in flame-sealed ampoules at various temperatures. In chemical stability the suspension should be subjected to an occasional shaking to check dispersability and drug solubility is analyzed by pH decomposition.[8]

b) Solution stability: These studies include the effect of pH, Ionic strength, Co-solvent, Light, Temperature and Oxygen. Usually these commence with probing experiments to confirm decay at the extremes of pH and temperature e.g., 0.1 N HCl, water and 0.1 N NaOH all at 90^0C. [9, 10]

c) Solid state stability: The primary objective of this study is investigation and identification of stable storage condition for drug in the solid state and identification of compatible excipients for a formulation. In all solid dosage formulation there will be some free moisture contributed by excipients as well as the drug and certainly in tablets a significant percentage typically 2% w/w is required for good compression. This free water has ability to act as a vector for chemical reaction between drug and excipients and the absorbed moisture films are saturated with drug compared to the dilute solutions encountered in injectables. Stability Testing of Pharmaceutical Products is first quantitative assessment of chemical stability of new drug.

It is defined as the capability of a particular formulation in a specific container or closer system to remain within its physical chemical, microbiological, therapeutic and toxicological specifications throughout its self-life Stability is officially defined as the time lapse during which the drug product retains the same properties and characters that is processed at the time of manufacture. The stability of a product is expressed as the expiry period or technically shelf life. Stability studies are important for the assurance to the patient, Legal Requirement and Economic Repercussions.[11] Purpose of stability study to ensure the efficacy, safety, quality of active drug substance and dosage forms, to establish shelf life or expiration period and to support label claims, to gain information about its packaging, assess the condition of the product on storage on prolong period of time, determine compatibility of drug with excipients and other additives and to determine the dosage form in which the drug is most suitable. **Table 2** describes types of stability and the condition maintained during the shelf life of the product. [12]

TABLE 2: TYPES OF STABILITY AND THE CONDITION MAINTAINED DURING THE SHELF LIFE OF THE PRODUCT

Types of stability	Conditions maintained during the shelf life of the product
Chemical	Retains its chemical integrity and labeled potency
Physical	Retains appearance, palatability, uniformity, dissolution and suspendability

Microbiological Retains sterility	effectiveness of antimicrobial agents
Therapeutic	Drug action remains unchanged
Toxicological	No significant increase in toxicity

CONCLUSION: After completion of preformulation evaluation of new drug candidates, it is recommended that a comprehensive report be prepared highlighting the pharmaceutical problems associated with molecules. It helps in developing phase I formulations and in preparing regulatory documents and aid in developing subsequent drug candidates. If, drug is found satisfactory sufficient quantity is synthesized to perform initial toxicity studies, initial analytical work and initial preformulation. Once past initial toxicity, phase I (clinical toxicology) begins for actual formulations. After that phase II and III clinical testing begins, and during this phase an order of magnitude formula is finalized. After completion of all above, an NDA is submitted and after approval of NDA, production can start.

ACKNOWLEDGMENTS: The author is thankful for library of Siddhant College of pharmacy, Pune for assistance and providing valuable data and knowledge in preparing this article.

REFERENCES:

1. Allen LV, Popovich NG and Ansel H.C:Ansels Pharmaceutical Dosage Forms and Drug Delivery Systems. Lippincott Williams and Wilkins, Wolters kluwer, New York, Edition 9, 2005: 431-492.
2. Vilegave K, Vidyasagar G and Chandankar P: Preformulation studies of pharmaceutical new drug molecule and products: An Overview. American journal of pharmacy and health research 2013; 1(3): 1-20.
3. Gaud RS, Yeole PG, Yadav AV and Gokhale S.B: Text book of pharmaceutics. Nirali Prakashan, Pune, Edition 12, 2011: 71-74.
4. Chein YW: Novel drug delivery systems. North corolina, Edition 2, revised and expanded, vol. 50: 381-528.
5. Gopinath R, Naidu RAS: pharmaceutical preformulation studies- current review. International journal of pharmaceutical and biological archives 2011; 2(5): 1391-1400.
6. Winfield AJ and Richards RME: Pharmaceutical practice. Churchill livingstone, Sydney Torento, Edition 3, 2004: 247-263.
7. Brahmankar DM and Jaiswal SB: Absorption of drugs in:. Biopharmaceutics and Pharmacokinetics A treatise. Vallabh Prakashan, Edition 1, 1995: 5-75.
8. Lachman L, Lieberman H A and Joseph L K: The Theory and Practice of Industrial Pharmacy. Varghese publishing house, Bombay, Edition 3, 1990: 171-196.
9. Banker GS and Rhodes CT: Modern Pharmaceutics. Revised and expanded, Marcel Dekker, Inc. Newyork, Edition 4, vol.121, 2008:167-185.
10. Vincent HK Li, Vincent HK Lee and Robinson JR: Influence of drug properties and drug administration on the design of sustained and controlled release system. Controlled drug delivery fundamental and applications. Marcel Dekker, New York, Edition 2, 1987: 3-61.
11. Kulkarni G T, Gowthamarajan B and Suresh B: Stability testing of pharmaceutical products-An overview. Indian Journal of Pharmaceutical Education 2004; 38(4): 194-198.
12. Jain NK and Sharma SN: A Text book of professional pharmacy. Vallabh prakashan, Pitampura Delhi, 2004: 317-333.

How to cite this article:
Chaurasia G: A Review on Pharmaceutical Preformulation Studies in Formulation and Development of new Drug Molecules. Int J Pharm Sci Res 2016; 7(6): 2313-20.doi: 10.13040/IJPSR.0975-8232.7(6).2313-20.