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A REVIEW ON "FOLMULATION DEVELOPMENT STUDIES"

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ABSTRACT

The term preformulation refers to a group of studies that focus on new drug candidates and physicochemical properties that could affect the medication's effectiveness and the creation of a dosage form.The need for molecular change or critical information for formulation design may be supported by this. The intrinsic chemical and physical properties of each medication were taken into consideration before creating a pharmacological formulation. This is a feature of the basis for mixing drugs with therapeutic ingredients to make dosage forms. Developing a dose form that is safe, dependable, palatable, and compatible with other substances is the aim of the preformulation analysis. Determining the novel pharmaceutical compounds' physicochemical characteristics is another goal. Among these characteristics are the medication's soluble content, partition value, rate of dissolution, polymorphic forms, and stability. No new medication is developed.

Keywords: Pre-formulation, Ercrucial-Information, Compounds, Medicine's Efficacy, Dissolution Rate.

I. INTRODUCTION

Drug development is a high trend in the pharmaceutical and Biotechnology industries. With growing responsibilities to study drugs candidates from discovery to human Clinical Trials as soon as possible, most pharmaceutical and biotech companies are providing a portion of the development of their potential new drugs. Outsourcing decrease the timeline of product development nd a cost-effective alternative. Changing needs of the people can be consider and fast solution can be provided to the company and people is necessary outsourcing gives a multiple cost structure, increasing resources and spending and decreasing when demand subsides.

Formulation can determine patentability, lifecycle the success of a pharmaceutical product. Companies use this formulation development rules and regulations and personnel into their product development to grow better. In large pharmaceutical companies, specific departments may exist as the physical Characterization of drug substances and formulation issues. In many cases, various department are work at deferent places so there handling is very much important by single authority so that the development get speed up and the formulation development timeline decreases. The concept of pre- formulation was known to us around 1950 as result of focus industrial pharmaceutical product development. it is stage of the pharmaceutical product development during which the physicochemical properties of the drug of drug substance are characterized and established the psychochemical and biopharmaceutical properties gives appropriate formulation and delivery methods

II. HISTORY

Ayurveda was developed by Dhanvantari, the Hindu legendary physician to the gods, who acquired knowledge of medicine from Brahma. The first known mention of it can be found in the Vedic text Atharvaveda. The German scientist Friedrich Serturner developed the first pharmaceutical medication in 1804.The first natural

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cures were found in plants, herbs, fungi, roots, vines, and other natural forms. Up until the middle of the nineteenth century, mankind had no other option for relieving pain except to use natural remedies. The first synthetic medication, chloral hydrate, was developed in 1869 and used as a sedative-hypnotic; it is still available today. The textile and synthetic dye businesses were closely related to the early pharmaceutical companies, and they were mirror copies of each other.

- **Definition:**

In pharmaceutics, pharmaceutical formulation is the process of combining various chemicals, including the active ingredient, to create a finished pharmaceutical product. Dosage form is typically included in the definition of the word formulation

STEPS IN FORMULATIONS:

1. **Identification and characterization of drug:**

The identification of characterization of drug is so much important because it very much affect the final product and also the effect of various characters make drug more potent or toxic.

2. **Excipients Compatibility Study:**

More the excipient compatible with drug more the chances of drug formulation success and effect of drug also increase.

3. **Formulation development:**

The next stage deals with the formulation development so that witch chemicals goes with witch and with excipients is suitable for drugs.

4. **Formulation Optimization:**

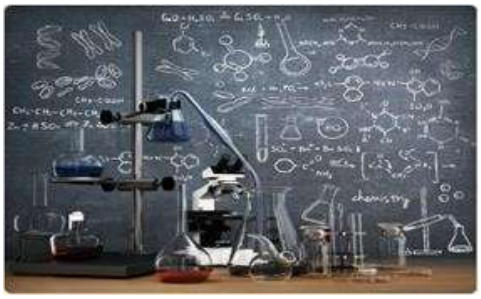
In this stage formulation like vaccine are produces this type of formulation have lots of studies than normal formulation and large amount of the knowledge needed.

5. **Formulation Evaluation:**

The evaluation studies help to improve the already, made formulation by changing the part of formulation like the vehicle types.

6. **Stability Studies:**

It deals with the stability of the formulation by doing various tests so that the stability of formulation increase it also helps to improve the shelf life of formulation.



FORMULATION OF CONVENTIONAL AND NOVEL DRUG DELIVERY SYSTEM:

1. **THE CONVENTIONAL DRUG DELIVERY SYSTEM:** The targeted release system releases the drug in dose form, while the drug delivery system absorbs the drug across a biological membrane. For example, tablets and capsules. Liquids for oral use. Semisolids, such as lotions, creams, and ointments, parenteral, etc. The traditional approaches to delivering medication to the body are called conventional DDSs. These approaches are typically employed more frequently when the objective is that the fast release of a medicine is necessary due to its rapid absorption. Among the traditional medication delivery methods are basic techniques that are oral, topical, inhalation, or injectable.

- **Tablet Composition:**

Usually, these comprise five to ten percent active ingredients, eighty percent inert substances, and ten percent compounds that aid in the breakdown of the item in the digestive system.

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- **Formulation of Capsules:**

In order to make a capsule, the active ingredient is enclosed in a "shell" composed of a substance that gels and dissolves in the intestines.

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- **Formulation of Oral Liquids:**

In addition to being quicker and less costly to create, liquid formulations frequently have higher bioavailability compared toother oral formulations.

- **Ophthalmic preparation:**

Ophthalmic preparations are specific dose forms intended for topical application, intraocular administration, perticular administration (such as just scleral or subtenon) administration, or us again conjunction with ophthalmic device.

Parental drug delivery:

Medication administered by means other than the digestive tract is referred to as a parentrally administered medication. Most commonly, the phrase "parenteral" refers to medication administered via injection or infusion.

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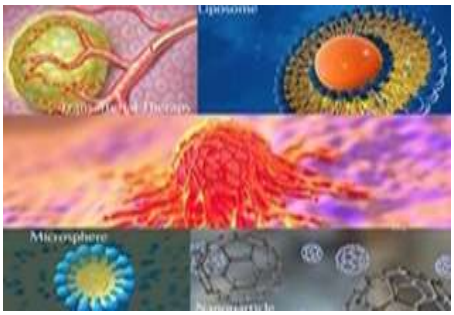
Generally speaking, the enteral route refers to ingesting medication.IM, IN, transdermal, Submucusal, subcutaneous (SC), IV, intraspinal, and intracapsule.

2. NOVEL DRUG DELIVERY SYSTEM: It is a novel approach to drug delivery that addresses the limitations of the traditional drug delivery systems controlled drug delivery system, Nano carriers, vesicular drug delivery system gastro retention drug delivery system.



A) CONTROLLED DRUG DELIVERY SYSTEM:

A controlled drug delivery system is aimed at releasing the correct dose of a therapeutic directly in the desired zone and during the required period of time.

TYPE: Diffusion Controlled, Dissolution Controlled

Mof: the fundamental principle for evaluation of the kinetics of drug release was offered by Noyes and Whitney in 1897 as the equation (10): dM /dt = KS (Cs ñ Ct)

III. NANO CARRIERS

Nano carriers are useful in the drug delivery process because they can deliver drugs to site-specific targets, allowing drugs to be delivered in certain organs or cells but not in others.

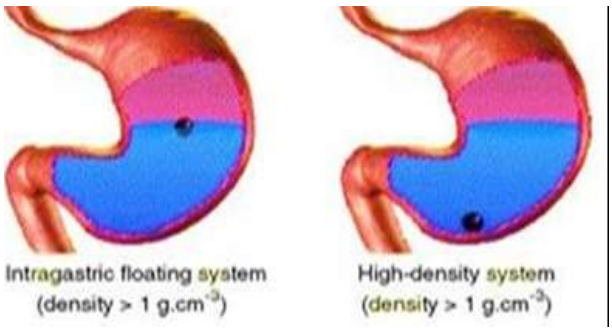
TYPE: liposomes, phytotosomes, nanoparticles, microsphere,

B) VESICULAR DRUG DELIVERY SYSTEM:

Vesicular drug delivery system is one of the systems that can improve the bioavailability of the drug and the reduction in toxicity by drug targeting to the specific site. Bingham pioneered the biologic origin of vesicular systems in 1965, and hence named them Bingham bodies.

C) GASTRO RETENTIVE DRUG DELIVERY SYSTEM:

Gastro retentive delivery systems are designed to be retained in the stomach for a prolonged time and release their active ingredients and thereby enable sustained and prolonged input of the drug to the upper part of the gastrointestinal (GI) tract ex Bio adhesive Drug, Expandable Drug, floating Drug, high density drug delivery.



D) NOSE BRAIN DRUG DELIVERY SYSTEM:

Nose to brain drug delivery system is an interesting approach to deliver a drug directly in the brain through the nose. Intranasal drug delivery is very beneficial because it avoids first-pass metabolism and achieves a greater concentration of drugs in the central nervous system (CNS) at a low dose. This delivery system is used for the treatment of various neurological disorders such as Parkinson's disease, Alzheimer's disease, schizophrenia, dementia, brain cancer, etc. To treat such types of diseases, different formulations like nanoparticles (NPs), micro emulsions, in situ gel, etc. can be used depending on the physiochemical properties of the drug.

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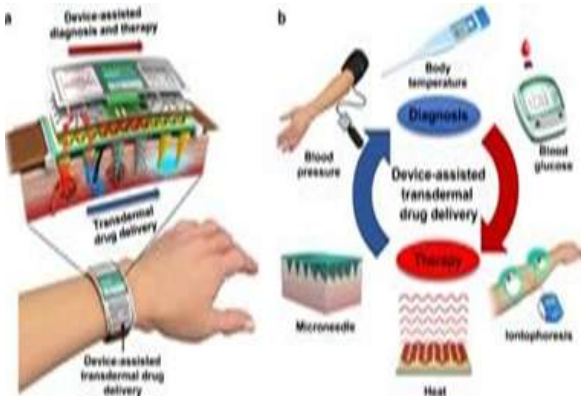
TRANSDERMAL DRUG DELIVERY SYSTEM AND IMPLANTS:

Transdermal drug delivery systems (TDDS), also known as "patches," are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin. The adhesive of the transdermal drug delivery system is critical to the safety, efficacy and quality of the product.



IV. EVALUATION TEST

Medication evaluation is a continuous activity. The review begins before a drug is dispensed, and continues during and after dispensing. A continuous review is crucial to identifying and resolving drug-related problem.

- **SOLID DOSAGE FORM:**

The solid dosage for needs various test of evaluation so that it shows popper properties of drugs.

DISSOLUTION TEST: The assembly consists of the following: vessel, which may be covered, made of glass or other inert, transparent material, which should not sorb, react or interfere with the preparation to be tested; a motor; a drive shaft; and a cylindrical basket (stirring element). The vessel is partially immersed in a suitable water-bath of any convenient size or heated by a suitable device such as a heating jacket. The water-bath or heating device permits maintaining the temperature inside the vessel at 37 ± 0.5 ºC during the test. Dis 30 min plain 60 min for capsules 30 min and vice versa if not disintegrate do again with 12, 16.

DISINTEGRATION TEST: To carry out a disintegration test for tablets, we use a basket which holds 1 to 6 tablets. This is then raised and lowered into a beaker of water, which is used to simulate conditions in the stomach at 3737 ± 0.5 ºC. If the tablets or capsules float, perforated plastic disks are placed on the top of the tablets to keep them under the water level. The tablet disintegration time is taken when no residue is left in the mesh. Disintegration Time: 6 solid dosage form in each tube for coated 15 min uncoated 30 min plain 60 min for capsules 30 min and vice versa if not disintegrate do again with 12.

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WEIGHT VARIATION TEST: To find out the uniformity in the weight, 20 tablets average weight bis calculated individual weight calculated, comparison is done Result's 30-N F 25 limits for weight variations case of tablet weighing up to 130±10% ,130/324±7.5%, 324 mg ±5%formula= w average – w initial/w average 8*1000.

DRUG UNIFORMITY TEST: 10 tablets powdered and 100 mg equivalence powder dissolve in suitable solvent make 100 ml solution and dilute it 100 time calculations are carried out**. Result:** Pass test when not less than 85 % and not more than 115%.

- **LIQUID DOSAGE FORM:** The liquid dosage for needs various test of evaluation so that it shows popper properties of drugs.

LEAKAGE TEST: 10 containers filled with liquid dosage form and inverted for 24 hours, also check for leakage in case of rubber closure.

DYE BATH TEST: To check ability of empty container or container with product , the container is deep in dye bath and pressure and vacuum applied to it and then after estimated time check for the dye marks.

CLARITY TEST: Dilute the preparations and check for cloudiness with control that is clean water in this test transparent particles or white particles observed against the black background and the black or dark particles observed against the white background.

STERILITY TEST: It is done for detecting the presence of viable forms of bacteria, fungi and yeast in parenteral products he test for Sterility must be carried out under strict aseptic conditions in order to avoid accidental contamination of the product during test.

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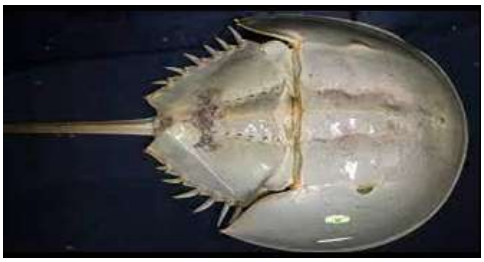
Two main types:

- **Direct transfer method**: Non filterable product test by this method test sample 10% →culture medium 9 ml tubes to 75 ml bottles →direct inoculum → incubate 14 days → M. growth →direct inoculum → incubate 14 days. → M. growth
- **Membrane filtration method:** sample →0.22 to 0.4 um pore size 47 mm diameter filter→ membrane cut into 2 halves → 100 ml culture medium →incubated 30 to 35 ºC 7 days →anther halve 20 to 25 ºC for 7 days.

PYROGEN TESTING : Pyrogens are metabolic product of the microbes produces fever with body each

- **Sham Test**: 3 rabbits→ 1 to 3 days observation →temp check 30 to 40 min prior → sample solution administration (37 ºC prior to injection) →thermometer in rectal cavity up to 7.5 cm →initial and second reading temp 0.2 c →1 Hr temp determine →do not vary from 1 ºC →rabbit shows 0.5 ºC rise test pass otherwise 5 additional rabbits are used.

- **Lal Test**: Limulus Amoebocytes Lysate (LAL) of limulus polymethyls gel is used 0.1 ml sample with the LAL reagent incubation for 1 Hr at 37 ºC clot is analysed due to properties of hours shoe crab gel.



- **SEMISOLID DOSAGE FORM:** The liquid dosage for needs various test of evaluation so that it shows proper properties of drugs.

PH MEASUREMENT: The pH is determine by means of the various methods like used of pH meter electrode measures the pH.

VISCOSITY MEASUREMENT: It measured by Instruments called "rheometers" and viscometer.

LABELLING AND PACKAGING: The primary function of packaging is to ensure the product is safe to transport, store, and sell, but labelling provides necessary information about the product using printed text, logos, artwork, or other designs.

Types of Packaging:

1. **Primary Packaging:** They have direct contact with drugs ex. cap liner label.

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2. **Secondary Packaging:** External to the primary packaging add additional physical protection, leaflets cartons etc.
3. **Territory Packaging:** Provides protection handling Warehouse storage and transportation ex brown cardboard boxes wood pallets etc.

- **Ampoules**: Vials, Containers, Strip package, Blister Packaging, Syringe, Dosing Doppler, Sachet, Packaging Containers, Aluminium foil, Injectables / Vials, Bottles, Cartons, Paper Board, Latitudes, Paper etc.
- **Airtight containers.** These containers prevent the contents from dust, moisture, and air**.**
- **Light resistant containers**. Multi-dose containers. Single-dose containers. Well closed containers. Aerosol containers. Child- proof containers etc.

Packaging Material:

- **Glass:** They are most commonly used for storing pharma products due to superior protecting quality.
- **Borosilicate glass type 1:**80 % silica 10% boric acid small amount of sodium oxide.
- **Soda lime glass:** Sulpher treatment more resistance than type 3.
- **Regular soda lime glass:** 75% silica 15% sodium oxide 10% calcium oxide
- **Products:** Colored glass ampules, bottles etc.
- **Plastic:** They contains one or more polymer together with additives desired shape can be given easily
- **Materials used:** Polyethene, polystyrene, polycarbonate, polyvinyl chloride, poly viny dine chloride polypropylene etc**.**
- **Metals:** Metals are more versatile of the all products that used Material used: Aluminium, tin, Products tablets, blisters, collapsible tubes cans, sachets, poches, membranes, etc.
- **Paper Paperboard:** They are traditional material used ever since ex boxes sachets etc.
- **Rubber**: They are used for closures stoppers and cap liners and bulbs

✓ **Type 1:** Most preferred strictest requirement.
✓ **Type 2**: Mechanical properties
✓ **Materials:** Natural, neoprene, nitryl, butyl, Chornobyl silicon.

- **Cotton:** It is used for wadding in solid preparations prevent collisional.
- **Films Foils Laminations:** They used to support barrier heat sealing decoration.
- **Adessive Links:** They used for labelling adhesion.

EVALUATION TEST FOR PACKAGING MATERIALS:

1) **Identification:** Appearance of packaging material alone and combination of the product content is checked
2) **Physical Test:** Appearance light absorption, ph., non-volatile matter, residue on ignition, heavy metals, buffering capacity, oxidable substances are check.
3) **Chemical Test:** Test include ph. materials chloride sulphates, paper or board, alkalinity of glass, compatibility test for containers.
4) **Mechanical Tests:** To check working and strength.
5) **Biological Test:** USP provides procedure for it implantation test, systemic injection test ,intracutaneous test**,**
6) **Environmental Test:** Materials test in environment.

EQUIPMENT AND INSTRUMENT HANDLING:

1. **Tablet Punching Machine:**

A pharmaceutical tablet press is a mechanical device that simplifies powders or granules into tablets of compatible size, shape and weight that contain roughly the same amount of excipient and active pharmaceutical

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ingredient. It is also referred to a s a tablet punching machine or tablet compression machine. Pharmaceutical powder formulations can be compressed into tablet form using a tablet press machine. The tablet compressing machine is another name for this device. Making tablets with consistent weight, size, and shape is highly helpful

2. Hardness Tester:

This test is also known as the "crushing strength test'. Tablet hardness has been is defined as the force required to break a tablet in diametric compression. The hardness is measured in kg/cm2.

3. Fribility Tester:

Friability test tells how much mechanical stress tablet are able to withstand during their manufacturing, distribution and handling by the customer.

%Friability = W1 - W2/W1×100

4. Disintegration Tester:

Disintegration is a process in which tablet are break up into granules or smaller particles. The U.S.P. device to test disintegration uses 6 glass tubes that are 3 inch long; open at the top and 10 mesh screen at the bottom end. One tablet is placed in each tube and the basket rack is positioned in a 1L beaker of water. Move the basket containing the tablet up and down through a distance of 5-6cm ata frequency of 28 to 32 cycle per minute.

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5. Dissolution tester:

Dissolution test used to throughout the life cycle of pharmaceutical product to evaluate the rate of release of a drug substance from the dosage form. Dissolution is considered one of the most important quality control tests performed on pharmaceutical dosage form. It is generally referred to as in vitro -in vivo correlation (IVIVC).

V. CONCLUSION

The formulation development studies along with the pre-formulation studies various tests and the sop handling are the important aspects of the pharmaceutical industries without this the industries cannot work properly and the quality efficiency and the new solution of the problems occurring during development cannot be solve one can know that the large amount efforts required with knowledge required for formulation development because "small mistake big consequences'.

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VI. REFERENCES

[1] A.B.A. Overguard, J. Moller-Sonnergaard, and L.L. Christrup, "Patients' Evaluation of Shape, Size, and Color of Solid Dosage Forms,"Pharm. World Sci. 23 (5), 185–188 (2001).

[2] Burke Marketing Research, "Consumer Attitudes Toward Solid Forms of Medication," BMR reports #48–203, March 1983.

[3] G.C. Cole and G. May, "The Instrumentation of a Zanasi LZ/64 Capsule-Filling Machine," J. Pharm. Pharmacol. 27, 353–358 (1975).

[4] L.E. Small and L.L. Augsburger, "Instrumentation of An AutomaticCapsule-Filling Machine," J. Pharm. Sci. 66, 504–509 (1977).

[5] A. Mehta and L.L. Augsburger, "Simultaneous Measurement of Force and Displacement in an Automatic Capsule-Filling Machine," Int. J.Pharm. 4, 347–351 (l980).

[6] J.W. Cropp, L.L. Augsburger, and K. Marshall, "Simultaneous Monitoring of Tamping Force and Piston Displacement (F-D) on an Hofliger-Karg Capsule-Filling Machine," Int. J. Pharm. 71, 127–136

[7] J.R. Britten and M.I. Barnet, "Development and Validation of a Capsule-Filling Machine Simulator," Int. J. Pharm. 71, R5–R8 (1991).

[8] P.K. Heda, F.X. Muller, and L.L. Augsburger, "Capsule-Filling Machine Simulation I: Low-Force Compression Physics Relevant to Plug Formation," Pharm. Devel. Tech. 4 (2), 209–219 (1999).

[9] G.L. Amidon et al., "A Theoretical Basis for a Biopharmaceutic Drug Classification: The Correlation of In Vitro Drug Product Dissolution and In Vivo Bioavailability," Pharm. Res. 12, 413–420 (1995).

[10] Turban, Expert Systems and Applied Artificial Intelligence (Macmillan Publishing Co., New York, NY, 1992).

[11] J.L. McClelland and D.E. Rumelhart, Explorations in Parallel Distributed Processing (MIT Press, Cambridge, MA, 1988).

[12] S. Lai et al., "An Expert System to Aid the Development of Capsule Formulations," Pharm. Tech. Eur. 8 (Oct.), 60–68 (1996).

[13] Capsugel Inc., Expert System for Formulation Support (Capsugel Library, Greenwood, SC, 1996).

[14] M. Caudill, "Expert Networks," in Neural Network PC Tools: A Practical Guide, R.C. Eberhart and R.W. Dobbins, Eds. (Academic Press,New York, NY, 1990), pp. 189–214.

[15] J.E. Botzolakis, "Studies on the Mechanism of Disintegrant and Surfactant Action in Encapsulated Dosage Forms,"PhD dissertation, University of Maryland, Baltimore, MD, 1985.

[16] USP 24–NF 19 (United States Pharmacopeial Convention, Inc. Rockville, MD), (2000).

[17] K.B. Shah, L.L. Augsburger, and K. Marshall,"An Investigation of Some Factors Influencing Plug Formation and Fill Weight in a Dosing DiskType Automatic Capsule-Filling Machine," J. Pharm. Sci. 75, 291–296 (1986).

[18] R.L. Carr, "Evaluating Flow Properties of Solids," Chem. Eng. 72,163–168 (1965).

[19] M.C.R. Johnson, "Particle-Size Distribution of the Active Ingredient for Solid Dosage Forms of Low Dosage,"Pharm. Acta. Helv. 47, 546–559 (1972).

[20] J.N. Staniforth,"Order out of Chaos," J. Pharm. Pharmaco. 39, 329–334 (1987).

[21] M.J. Crooks and R. Ho, "Ordered Mixing in Direct Compression of Tablets," Powder Tech. 1, 161–167 (1976).

[22] J. Verraes and R. Kinget, "Ordered Powder Mixing: Theory and Practice," Int. J. Pharm. Tech. Prod. Mfr. 1 (3), 36–41 (1980).

[23] D.A. Piscitelli et al., "The Impact of Formulation and Process Changes on In Vitro Dissolution and Bioequivalence of Piroxicam Capsules," Pharm. Devel. Tech. 3 (4), 443–452 (1998).