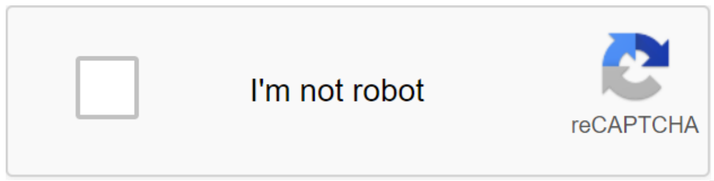

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Biopharmaceutical factors affecting drug bioavailability pdf

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How is it different from BIOEVIZATION? If two or more, similar forms of dosage of the same drug reach circulation at the same relative rate and expand, it is a bioekuvalent drugs of this generic drug. The difference in bioavailability is usually observed with oral dosage forms, the bioavailability of I.V is 100%, I.M and S.C are thought to be close to 100%. Differences of less than 25% in bioavailability between multiple formulations of a single drug usually do not have a significant effect on the clinical outcome, hence such formulations can be called BIOE-4ALENT. 5. Chemical equivalence - If two or more forms of dosage of the same drug contain the same labeled quantities of the drug as indicated in Pharmacopeia, these are chemical equivalent drugs. Pharmaceutical equivalence - If two or more chemical equivalent forms of the drug also contain other similar ingredients, such as excipients (binders), these dosage forms are considered the pharmaceutical equivalent. 6. Therapeutic equivalence - If they provide identical in vivo pharmacological responses, as measured by symptom control or disease and safety profile. Clinical Equivalence - If one structurally different drug can provide the same clinical response as another mechanically related drug, they are considered to exhibit clinical equivalence. 7. What are the factors influencing BIOVILITAGY? Pharmaceutical Factors - Pharmacological Factors 8. Pharmaceutical Factors: - It is expected that the bioavailability of medicines will be in this reduced order - Pharmaceutical factors include: - Particle size - the rate at which the drug dissolves be increased by increasing its surface area by reducing its PARTICLE SEE. - Salt form - the speed at which Salt dissolves is different from its parent connection. Salts of low-acid drugs are very water-soluble, free acidic drugs are sucked out of these microcrystal salts, which has a faster dissolution rate and increases bioavailability. - Crystal forms - The rate of absorption and bioavailability of the drug also depends on its crystalline shape. This is because amorphous forms dissolve faster than crystalline forms, because there is no energy needed to break up the crystal lattice, thereby increasing their bioavailability. 10. - Water hydration - Many drugs include water for the production of a crystalline form called hydrates. If water molecules are already present in the crystal structure, the tendency of the crystal to attract additional water to initiate the dissolution process decreases compared to the anhydrouse forms. - Nature excipients and Adjuvants - These pharmacologically inert substances (e.g. starch, lactose, calcium sulfate, gums) that are added as material filler or as binding substances or to obtain proper granular size, have a huge impact on the bioavailability of the drug. Some of these excipients are wetting agents that increase solvent penetration and provide faster dissolution and in turn absorption. We need to be especially careful in drugs that follow zero order or mixed-order kinetics or have a low margin of safety. - Degree of ionization - Non-ionized, lipid soluble drugs are better absorbed, increasing their bioavailability, compared to highly acidic or highly essential drugs or highly ionized drugs. 11. Pharmacological factors: 12. Pharmacological factors include: - emptying of the stomach and gastrointestinal mobility - Factors that accelerate the emptying of the stomach increases bioavailability. This is due to the fact that the drug is exposed to a larger area of the surface of the small intestine. - Gastrointestinal diseases - There are many gastrointestinal diseases that affect the absorption of the drug, the outcome of coeliac disease is complex, it increases the absorption of cephalexin, while reduces amoxicillin. In the case of Crohn's disease, there is a disproportionate absorption of individual components of cotrimocsazole, increased absorption of sulphamethoxazole, reduced trimethoprim - food and other substances - in general, the rate of absorption of GI is reduced after meals, although does not affect the extension of absorption. Both the rate and the increase in the absorption of certain antibiotics, such as rifampicin, decrease after eating. 13. The absorption of tetracyclion decreases when taken with milk because it forms poorly digestible calcium complexes. Vit. C increases iron, because it keeps it in the shape of an iron. - First Pass Metabolism - This means that drug degradation occurs, reducing its bioavailability when it has gone through the GIT wall and then then portal system before it reaches systemic circulation. The interaction between drugs and drugs and drug interactions can also lead to a difference in bioavailability. - Liquid paraffin reduces the bioavailability of fat-

soluble vitamins because it emulsifies fat. Antacids reduce the bioavailability of tetracyclines, as they form a chelatized complex. - Pharmacogenetic factors - A big difference in bioavailability often occurs in people for pharmacogenetic reasons. Slow and fast acetylators show increased and reduced bioavailability of isoniazid, respectively. 14. - Various factors - The area of the absorption surface - the state of circulation at the site of absorption (shock, with a decrease in tissue perfusion) - the route of administration 15. Inquiries: - Goodman L.S., Goodman and Gilman's Pharmacological Therapy Foundation, 13th edition, New York; New Delhi, TataMcGraw-Hill Education, 2017. - Katzung B. G, Basic and Clinical Pharmacology, 14th edition, New York; New Delhi, TataMcGraw-Hill Education, 2017. - Tripathi K.D., Basics of Medical Pharmacology, 7th Edition, New Delhi, Jaypee Brothers Publications, 2013. - Sharma H. L., Principles of Pharmacology, 3rd edition, New Delhi, Paras Medical Publisher, 2018 16. Thank you! ⏮ 1. PRESIDENCY BY CHIRANJIBI ADHIKARI M. Pharm. 1st year OF THE 1st YEAR TO MR. KEERTHY H.S. M. Pharm. Professor of Pharmaceuticals, Mallige College of Pharmacy. #71, SILVEPURa, BANGALORE: 560 090 2. Biopharmaceuticals is the study of the physical and chemical properties of the drug and the drug in vitro, on the bioavailability of the drug in vivo, to obtain the desired therapeutic effect. Biopharmaceuticals makes it possible to rationally develop medicines. The main problem of biopharmaceuticals is the bioavailability of medicines. Bioavailability refers to the measurement of the speed and degree of the active drug, which become available at the site of action. 3. ⚠ Biopharmaceutical factors influencing the bioavailability of medicines Biopharmaceuticals considerations in the development of a drug for the delivery of an active drug with the desired characteristics of bioavailability include: 1. Type of medicinal product (e.g. tablet, capsule, transdermal delivery system, topical ointments, parenteral solution), 2. The route of the introduction of the drug, including the anatomical and physiological nature of the place of application (e.g. oral, topical, injectable, implant, transdermal patch, etc.), 3. The desired pharmacodynamic action (e.g. immediate or prolonged activity), 4. The physical properties of the drug molecule, 5. The character of excipients in the drug product, and 6. Manufacturing method. 4. In each drug use route there are special biopharmaceutical considerations in the development of medicines. For example, in the development of a vaginal pill for treatment infections should be used ingredients compatible with vaginal anatomy and For an extrasuscular drug (e.g. intramuscular injection), local irritation, dissolution of the drug and absorption of the drug from the intramuscular area are among the factors that need to be considered. If the drug is given in an intravascular way (e.g. drip injection), systemic absorption of the drug is considered complete or 100% bioavailable, as the drug is placed directly in the general circulation. 5. Some drugs have poor bioavailability due to first-aisle effects (pre-systemic elimination). If the bioavailability of the oral drug is bad due to the metabolism of enzymes in the gastrointestinal tract or in the liver, then a higher dose may be required, as in the case of proranolol, or an alternative route of administration of the drug, as in the case of insulin. If the bioavailability from the solid form of the dosage is lower than that of the oral solution, the performance of the dosage form can be improved by reformulation. Low bioavailability from oral solution, on the other hand, indicates that the drug is poorly digested or prone to significant metabolism of the first passage and is unlikely to be improved by development. Increased stomach emptying usually increases the bioavailability of drugs administered orally. 6. Formulations and production variables that may affect the bioavailability of a drug product 1. Properties of the drug (salt form, crystalline structure, formation of solvites and solubility). 2. The composition of the finished form of dosage (the presence or absence of excipincists and special coatings). 3. Manufacturing variables (tablet compression force, variable processing, drug or extreme particle size, and environmental conditions). 4. Assess and/or place of dissolution in the gastrointestinal tract. 7. ⚠ speed limit in drug absorption - Systemic absorption of the drug from a drug product consists of a sequence of speed processes. For solid oral, immediately released drugs (e.g. tablets, capsules) the rate of processes includes: - (1) the breakdown of the drug and the subsequent release of the drug, (2) the dissolution of the drug in the environment and (3) absorption through cell membranes in systemic circulation. In the process of decay, dissolution and absorption of the drug, the rate at which the drug reaches the circulatory system is determined by the slowest step in the sequence. The slowest step in a series of kinetic processes is called the speed limit step. 8. With the exception of controlled release products, the breakdown of a solid oral drug tends to occur faster than drug dissolution and drug absorption. For drugs that have very poor aqueous solubility, the rate at which the drug dissolves (dissolving) is often the slowest step hence has a speed-limiting effect on the bioavailability of drugs. In contrast, for a drug that has a high aqueous aqueous The dissolution rate is rapid, and the rate at which the drug crosses or permeates the cell membranes (absorption) is the slowest or most speed limiting step. Figure 1- Evaluate the bioavailability processes of drugs 9. DISINTEGRATION - For the immediate release of solid forms of oral dosage, the drug must break down into small particles and release the drug. Complete disintegration is defined by USP as a state in which any residue of the tablet, except for fragments of insoluble coating left on the test vehicle screen in a soft mass, does not have a palpably solid core. - Although break-up tests allow accurate measurement of the formation of fragments, pellets or aggregates from solid forms of dosage, no information from these tests about the rate of dissolution of the active drug has been received. Solid medicines exempt from disintegration include trosi, chewing tablets, and medicines designed for sustained release or long-term or re-effects. 10. SOLUTION AND SOLULICIA is a dissolution process in which a solid drug is dissolved into solvents. Soluble is the mass of dissolution, which dissolves in a certain mass or volume of solvent at this temperature (for example, 1 g NaCl dissolves in 2,786 ml of water at 25 degrees Celsius). Solubility is a static property; while dissolution is a dynamic property. The rate at which drugs with poor acute dissolution dissolve from the untouched or decaying solid form of dosage in the gastrointestinal tract often controls the rate of systemic absorption of the drug. Thus, dissolution tests can be used to predict bioavailability and can be used for discriminatory formulations that affect the bioavailability of drugs. 11. Noyes and Whitney (1897) and other researchers studied the rate at which solid drugs were dissolved. Steps in dissolution include the process of dissolving the drug on the surface of the solid particle, thus forming a saturated solution around the particle. The dissolved drug in a saturated solution, known as a stagnant layer, is scattered into the bulk of solvent from regions with high concentrations of drugs to regions with low concentrations of drugs. Figure 2 - Dissolving the solid part of the drug into solvents. C s - concentration of the drug in a stagnant layer, C - concentration of the drug in bulk solvents. 12. The overall rate of dissolution of the drug can be described by the equation Noyes Whitney- Where, dC /dt - the rate of dissolution of the drug during t, D - the rate of diffusion constant, A - surface particle area, C s - the concentration of the drug (equal to the soluble of the drug) in the stagnant layer, C - the concentration of the drug in solvents, and h-thickness. The rate of dissolution, dC /dt , is the rate of the drug dissolved at a time expressed as a change in concentration in the dissolution of the liquid. 13. - Increase The temperature will increase the kinetic energy of the molecules and increase the constant diffusion, D. In addition, the increase in the agitation of the solvent environment will reduce the thickness, h, stagnant layer, allowing faster dissolution of the drug. The drug in the body, especially in the gastrointestinal tract, is considered to dissolve in the aquier environment. The piercing of the drug through the intestinal wall (model of the lipid membrane) is affected by the ability of the drug to diffusion (D) and to the septum between the lipid membrane. The favorable section factor (K oil/water) will facilitate the absorption of the drug. 14. Factors influencing the dissolution of the drug - Factors that affect the dissolution of the drug in a solid form of oral dose, include (1) the physical and chemical nature of the active drug, (2) the nature of the exicients and (3) the method of production. 15. 1. The physiochemical nature of the drug The physical and chemical properties of the drug, as well as the nascent ones are important considerations in the development of the drug product. For example, intravenous solutions are difficult to prepare with drugs that have poor solubility. Drugs that are physically or chemically unstable may require special excients, coatings or production processes to protect the drug from degradation. The powerful pharmacodynamic activity of drugs such as estrogen and other hormones, penicillin antibiotics, chemotherapy agents of cancer and others can cause adverse reactions of staff who are exposed to these drugs during production. 16. ⚠ solubility, pH and absorption of drugs - the main drug is more soluble in acidic environment, forming soluble salt. Conversely, the acidic drug is more soluble in the intestine, forming soluble salt at a more alkaline pH. The pH soluble profile gives an approximate estimate of the completeness of dissolution for the dose of the drug in the stomach or in the small intestine. Soluolity can be improved with the addition of sour or basic excipient. For example, the soluble of aspirin can be increased by adding an alkaline buffer. In the development of controlled release drugs, buffer agents can be added to slow down or change the rate at which the fast-dissolved drug is released. 17. ⚠Stayness, pH and absorption of drugs - If the decomposition of the drug occurs with the help of acid or basic catalysis, some prediction of the degradation of the drug in the gastrointestinal tract can be made. For example, erythromycin has a stability profile that depends on pH. In an acidic environment, as in the stomach, erythromycin decomposes quickly, while in neutral or alkaline pH the drug is relatively stable. Consequently, erythromycin tablets are enteric coating to protect against acid degradation in the stomach. The level of dissolution of erythromycin powder ranged from 100% dissolved within 1 less than 40%, dissolved in 1 1 Dissolving powdered raw materials is a very useful in vitro method for predicting the bioavailability problems of erythromycin product in the body. 18. ⚠ particle size and drug absorption - Since dissolution occurs on the surface of the soluble (medication), the larger the surface area, the faster the rate of dissolution of drugs. Griseofulvin, nitrofurantoin, and many steroids are drugs with low aqueous solubility; reducing the size of particles by milling to a micronized form has improved the oral absorption of these drugs. The smaller size of the particles increases the total surface area of the particles, increases the penetration of water into the particles and increases the rate of dissolution. For poorly soluble drugs, a diintreant can be added to the compound to ensure rapid breakdown of the pill and release of particles. Adding surface-active substances can increase wetting as well as solubility of these drugs. 19. Polymorphism, hydrates and drug absorption - Some polymorphic crystals have much lower solubility than amorphous forms, resulting in the product being incompletely absorbed. Chloramphenicol, for example, has several crystalline forms, and in oral suspension the concentration of the drug in the body was established dependent on the percentage of polymorphs in suspension. Some polymorphs are metastable and can be transformed into a more stable form over time. For example, changing the crystalline structure of the drug can lead to cracking in the tablet or even prevent the compression of granulation into the tablet. Water can form special crystals with drugs called hydrates; for example, erythromycin hydrates have a completely different solubility compared to the anhydrotic form of the drug. It has been found that ampicillin trihydration is less digestible than the anhydroous form of ampicillin, due to the faster dissolution of the latter. 20. 2. The nature of excipients in the drug product - Excipients in the drug product affects the kinetics of drug dissolution, or by modifying the medium in which drugs dissolve or by reacting with the drug itself. Pausing agents to increase the viscosity of a drug vehicle and thereby reduce the rate of dissolution of drugs from suspensions. Excessive amounts of magnesium stearat (hydrophobic lubricant) in the tablet can repel water and slow the dissolution of the drug and slow down the rate of absorption of the drug. Coatings, especially shells, will intersect when aging and reduce the rate of dissolution. 21. Low concentrations of surfactants reduce surface tension and increase the rate of dissolution of the drug, while higher concentrations of surfactants tend to form micelles with the drug and thus reduce the rate of dissolution. Emitted, such as sodium bicarbonate, can alter the pH of the environment, active drug. Aspirin, a weak acid when formulated with sodium bicarbonate, will form water-soluble salt in an alkaline environment in which the drug dissolves quickly. The radiationed composition can interact directly with the drug to form a water-soluble or water-soluble complex. For example, if tetracycline is formulated with calcium carbonate, an insoluble complex of calcium tetracycline is formed, which has a slow rate of dissolution and poor absorption. 22. 3. Manufacturing method - High compression of tablets without sufficient dissonant can lead to a bad breakdown of the compressed tablet. In some cases, the drug is designed so that it can be used in conjunction with a specialized medical device. For example, a drug solution or suspension may be designed to work with a nebulizer or dose dispenser for administration in the lungs. Both the physical characteristics of the nebulizer and the composition of the drug can affect the particles of droplets and the pattern of spraying, which the patient receives when inhaling the drug. The bioavailability of the drug from various forms of dosage will decrease in the solution of the order, suspension and capsule, tablet with coating 23. Links 1. Applied Biopharmaceuticals and Pharmacokinetics, 6th edition, Leon Chargel, Suzanne Wu-Pong, Andrew B.K. Yu, Page 361-398. 2. Theory and Practice of Industrial Pharmacy, 4th Edition, Lachman and Lieberman, page 303. 3. Bioavailability: Pharmaceutical Review, Ahmed N.Allam, Safaa S.El Gamal, Vivian F.Naggar, Int J Roman Drug Deal Tech 2011:Vol.1:Issue 1 biopharmaceutical factors affecting drug bioavailability pdf