IMPACT OF DRUG POLYMORPHISM ON THE PROCESS OF DRUG RELEASE FROM THE DOSAGE FORM

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Introduction. Many pharmaceutical substances form polymorphic modifications with different physical properties. The phenomenon of polymorphism of pharmaceutical substances can sometimes be extremely useful, as it makes it possible to regulate the rate of release of the substance from the dosage form, and in some cases leads to a decrease in the therapeutic activity of the drug. Therefore, studying the impact of polymorphism on the quality of dosage forms is an important issue for the pharmacist technologist.

Polymorphism (from Greek πολύς "many" + μορφή "form"), is the phenomenon of the same substance existing in several different crystalline forms. Solids have long been divided into crystalline and amorphous. X-ray diffraction analysis, however, shows that most of the so-called amorphous substances have a crystalline lattice. A crystal is a solid, whose particles (atoms, ions) are arranged in a certain, periodically repeating order, forming a crystalline lattice.

The phenomenon of polymorphism was discovered in 1822 by E. Mitchenlich (the essence of polymorphism consists in the fact that under certain conditions certain substances can form crystals of different symmetry and shape. Each of the crystal shapes that form as a result of polymorphism is called a polymorphic modification. Polymorphic modifications of a substance have a peculiar geometric crystal form. The phenomenon of polymorphism, characteristic of crystals, is common also for crystalline medicinal substances. Almost all substances can be obtained in different polymorphic modifications under certain conditions.

The shape of crystals depends on the conditions of growth and the nature of the substance. The growth and shape of crystals is influenced by the temperature at which crystallization occurs, the presence of impurities in solutions, the solvents from which the substance is crystallized, the position of the crystal during growth, etc.

The shape of the crystals changes particularly strongly under the influence of impurities in the mother liquor. The impurities either impurities either adsorb on the surface (occlusion) or penetrate into the crystal (occlusion). In both cases the shape of the crystal may change in the presence of impurities. In both cases the shape of the crystal may change.

During polymorphic transformation the type of chemical bonding in the crystal changes to a greater or lesser extent, the crystal angles and its physical and chemical properties change dramatically, as well as its pharmacological properties.

The aim of the study. To study the dependence of drug polymorphism on the release process of drugs from dosage forms using two antidiabetic drugs as examples: amorphous and crystalline zinc-insulin.

Methods of research. The objects of the study were two insulin preparations: zinc-insulin amorphous and crystalline, widely used in medical practice for diabetes mellitus. The experiment is conducted for training purposes, and three animals (white rats) of equal weight after an 18-hour fast may be used as an exception. The animals

are divided into three groups and their initial blood glucose concentration is determined. After this two animals are injected subcutaneously with zinc-insulin amorphous and zinc-insulin crystalline respectively at a dose of 1.0 units/kg. A third animal is the control animal. Blood glucose concentration of the animals was determined after 1, 2 and 3 hours from the start of the experiment. Blood glucose concentration (mol/L) was determined by a calibration curve constructed using a standard glucose solution or by data.

Main results. In the "in vivo" experiment, it was found that the administration of insulin preparations decreases the blood glucose concentration of animals, the hypoglycemic effect being more pronounced under the influence of amorphous zinc-insulin than crystalline zinc-insulin.

Conclusions. It has been shown that the rate of insulin release from preparations depends on their physical properties, in this case due to zinc-insulin polymorphism.

BIOAVAILABILITY OF MEDICINAL SUBSTANCES

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Introduction. Studies of the last three decades conducted by domestic and foreign scientists using modern physic-chemical, pharmacological and biochemical methods have allowed sufficiently deep and reliable understanding of the complex relationships that have developed between the drug as a special physic-chemical system, and the macro-organism as a biological system of the factors that cause these relationships. The criterion for assessing the degree of influence of individual or the sum of pharmaceutical factors on the activity of a medicine is the testomological (physiological) availability of the drugs. Bioavailability actually describes the quality of a medicine.

The aim of the study. To study the basic principles of drug bioavailability, which is an indispensable link in biopharmacy.

Methods of research. The measure of bioavailability (BA) is the ratio (in percent) of the amount of a drug substance absorbed prescribed in the investigational dosage form (S) to the amount of the same drug substance prescribed in the same dose but in the standard dosage form (S1). The bioavailability can be determined using the following formula: BD=S*100/S1.

Main results. The standard dosage form is intravenous injection as it ensures immediate and complete entry of the drug into the large circulatory system. In this way, absolute bioavailability is determined. It is more common, and probably more useful, to determine relative bioavailability. For this purpose, the standard dosage forms are a solution or other oral dosage form that is well characterized and well absorbed.

The bioavailability is usually determined by determining the excretion of the drug in the urine (over a known period of time after administration) or the concentration of the drug in the blood after a single or multiple administration. However, there are medicines whose bioavailability needs to be determined differently, such as when applied to the skin (ointments, liniments, plasters) or to the rectal mucosa