



Drug technology department
Discipline "Biopharmacy"



Pharmaceutical factors and their impact on therapeutic efficacy of drugs. Influence of adjuvants nature on the process of releasing an active pharmaceutical ingredients from drugs.

**LECTURE FOR ENGLISH SPEAKING STUDENTS
OF SPECIALTY «PHARMACY»**

Lecturer: *ass. prof. Kovalev V.V.*

PLAN OF THE LECTURE

- 1 **Pharmaceutical factors**
- 2 **Classification of pharmaceutical factors**
- 3 **Simple chemical modification of drugs**
- 4 **Auxiliary substances**
- 5 **Type of medicinal form and the way of its administration**
- 6 **Technological process**

Questions for individual work

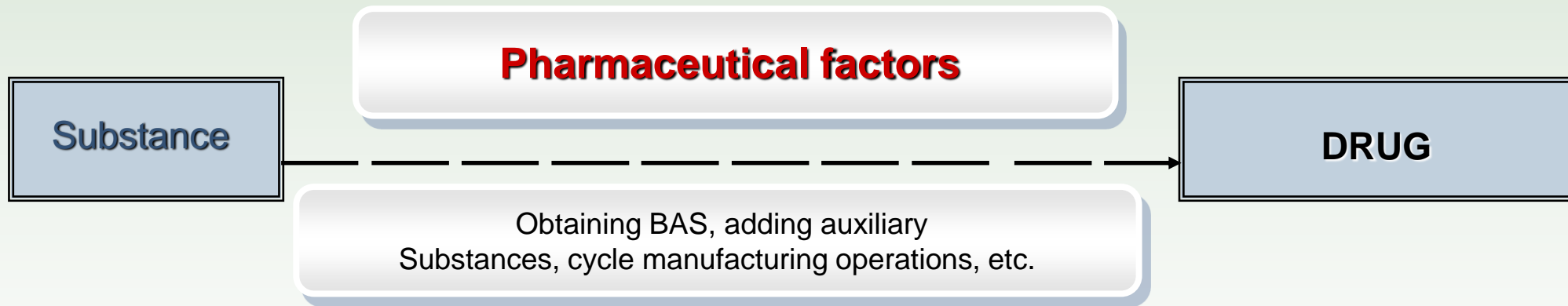
- 1. Types of chemical bonds that arise between active substances and excipients.***
- 2. Factors affecting the rate of resorption of active substances.***

Recommended Books

- Biopharmaceutics. Practical handbook for English students of the 5th year, speciality “Pharmacy”: a handbook for the work of students / Edited by acad. A.I. Tikhonov. - Kh.: PH of NUPh, 2011. – 68 p.
- British Pharmacopoeia. – London: The Stationery Office, Vol. III, 2009. – P. 7533-7614. European Pharmacopoeia. Sixth edition. – Strasbourg: Council of Europe, Vol.1., 2008. – P. 1063-1084.
- Shargel, L. Applied Biopharmaceutics & Pharmacokinetics / L. Shargel, A. Yu, S. Wu-Pong. – 6 ed. – New-York: McGraw-Hill Medical, 2012. – 811 p. Mark P. Mathieu. PAREXEL Biopharmaceutical R&D Statistical Source-book 2014-2015 / Mark P. Mathieu. – Parexel Intl Corp., 2014. – 421 p.
- www.tl.nuph.edu.ua – site of Drugs Technology Department.
- Training portal <http://pharmel.kharkiv.edu> – distance learning center of NUPh.
- <http://dspace.nuph.edu.ua> – electronic archive of NUPh.

PHARMACEUTICAL FACTORS

Pharmaceutical factors - any factors that has influence on the drug during the manufacturing of the drug and has affect on its therapeutic efficiency



The influence of pharmaceutical factors should be taken into account at all stages of the drug preparation - from getting the effect of biologically active substances to the packaging of finished products

PHARMACEUTICAL FACTORS

Pharmaceutical factors

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graph TD; A[Pharmaceutical factors] --> B[most significant effect on therapeutic efficiency of drugs]; A --> C[could cause therapeutic drugs inequivalence]; A --> D[can be changed during the development of drugs for the purpose of creating drugs preset properties];
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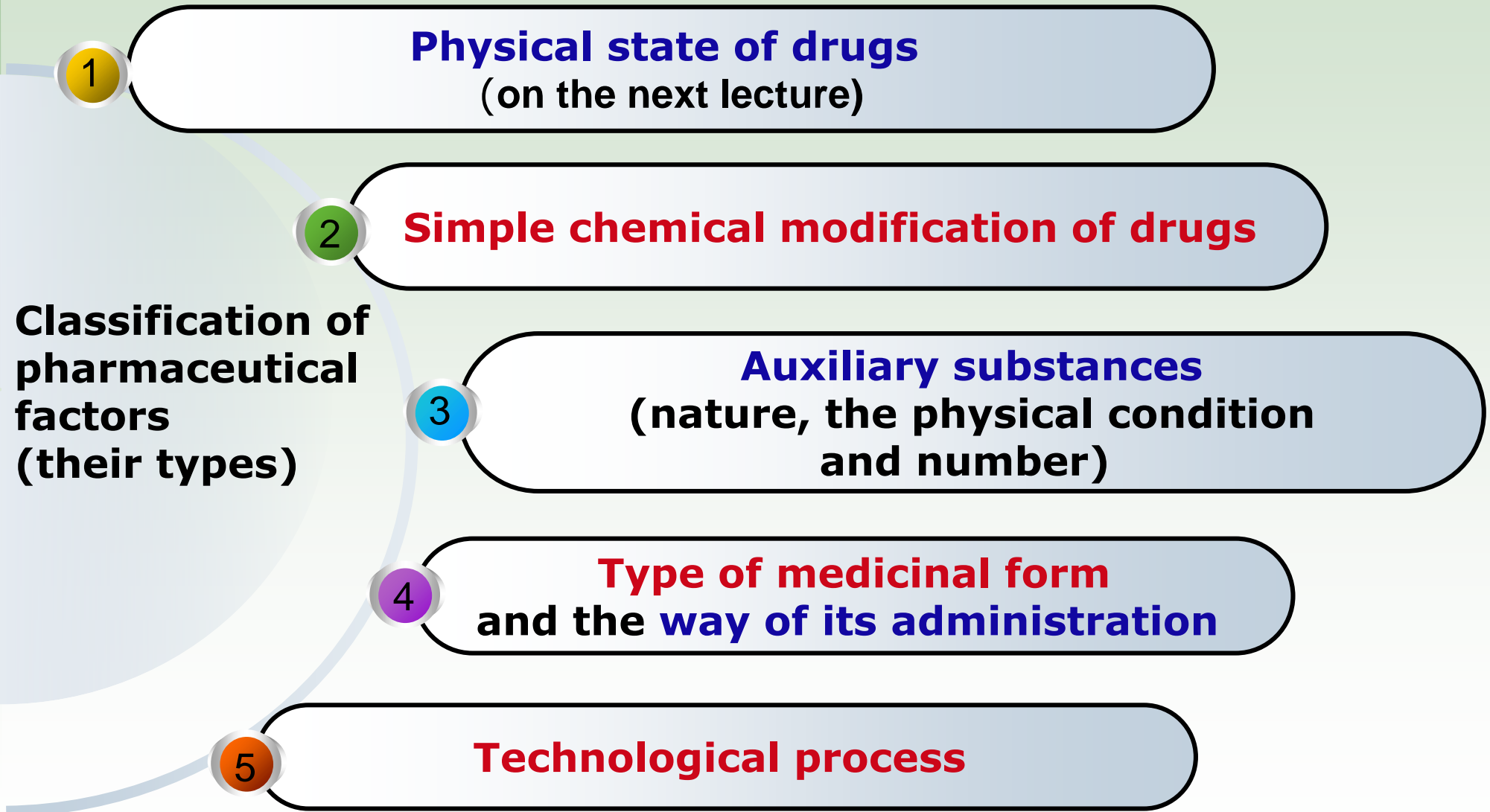
most significant effect on therapeutic efficiency of drugs

could cause therapeutic drugs inequivalence

can be changed during the development of drugs for the purpose of creating drugs preset properties

- **Rational choice of pharmaceutical factors in the manufacture drugs can provide maximum therapeutic efficiency of the active ingredient at a minimum possible side effects**

CLASSIFICATION OF PHARMACEUTICAL FACTORS



SIMPLE CHEMICAL MODIFICATION OF DRUGS

A simple chemical modification

The same active ingredient can be incorporated into the drug in the form of various chemicals (salt, base, acid, ester, complex compound, etc.), that fully retains responsibility for the pharmacological effect of the molecule substance (pharmacophore)

novocaine - base and novocaine hydrochloride - salt;
codeine - base and codeine phosphate - salt;
Caffeine - base and caffeine sodium benzoate - salt;
Phenobarbital - base and phenobarbital sodium - salt;
norsulfazol - base and norsulfazol sodium - salt

SIMPLE CHEMICAL MODIFICATION OF DRUGS

A simple chemical modification of drugs commonly used in the creation of drugs: uses the chemical modification of the drug, which provides the best therapeutic effect.

Advantages:

- increase the effectiveness of drug therapy
- reduce the dose of drug
- increase the stability of many drug substances and their preparations

Using different drug types in pharmacotherapy is done by converting the **molecular mass** or **units of action**

Example:

codeine phosphate (salt) 1.0
codeine ($\overline{\text{base}}$) 0.75

AUXILIARY SUBSTANCES

Auxiliary substances -
any component of the drug, with the exception of
active substances

Classification of
auxiliary
substances



Nature



Synthetic



Semisynthetic

AUXILIARY SUBSTANCES

Auxiliary substances in drug

**Provide retrieve certain drug form.
Function as:**

- Solvents
- Thickening agents
- Fillers
- Emulsifiers
- Stabilizers
- Bases for ointments and suppositories
- Antioxidants
- Preservatives
- Flavoring agents
- Dyes etc.

Has influence on the pharmacokinetics of the drug:

- Release
- Absorption
- Distribution
- Metabolism
- Excretion

AUXILIARY SUBSTANCES

- **Biopharmaceutical research has shown that auxiliary substances significantly affects on therapeutic efficiency of drugs**

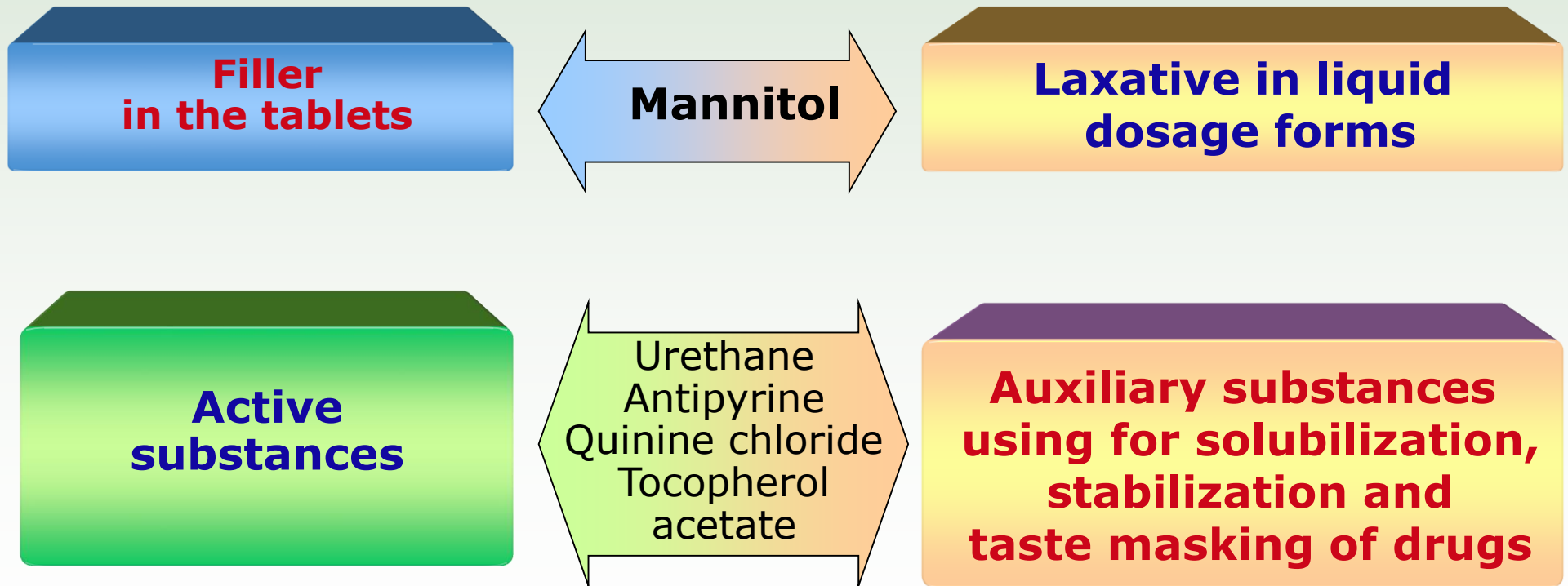
Auxiliary substances can:

- **Increase**
- **Reduce**
- **Modify**

the pharmacological effects of drugs

AUXILIARY SUBSTANCES

Separation of the drug components to active and auxiliary substances greatly arbitrary. With a certain composition auxiliary substances become active and active become auxiliaries



AUXILIARY SUBSTANCES

The choice of auxiliary substances should be based primarily biopharmaceutical, and then the technological, economic and other indicators

Auxiliary substances should provide for drugs

Obtaining the required drug form suitable for application, storage, transport, etc.

Maximum therapeutic effect with minimal side effects

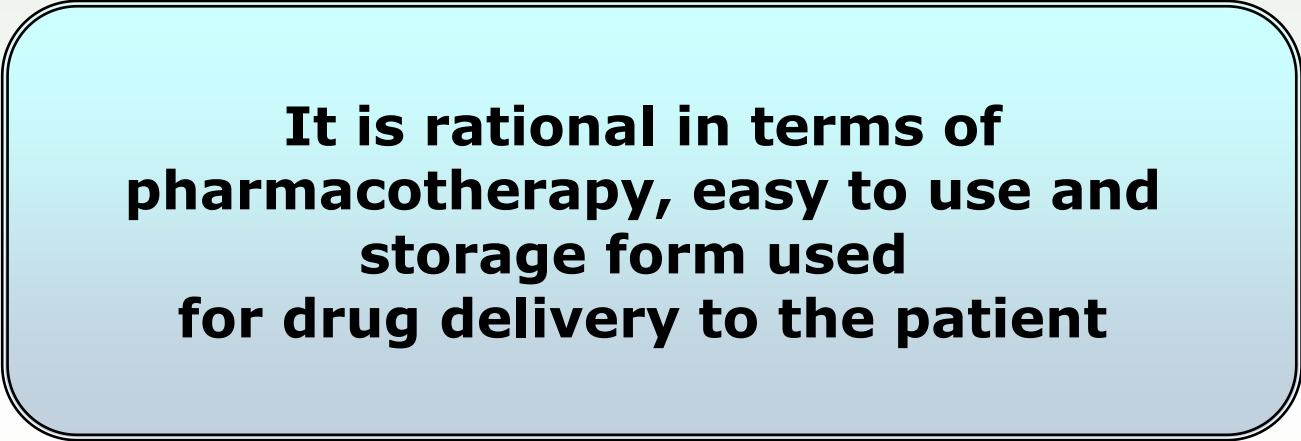
TYPE OF MEDICINAL FORM **AND THE WAY OF ITS ADMINISTRATION**

The same drug can be administered to the patient in various dosage forms and in different ways:

- per os - in the form of powders, capsules, pills, potions;**
- external - in the form of ointments;**
- parenterally - in the form of injection solutions;**
- sublingual, etc.**

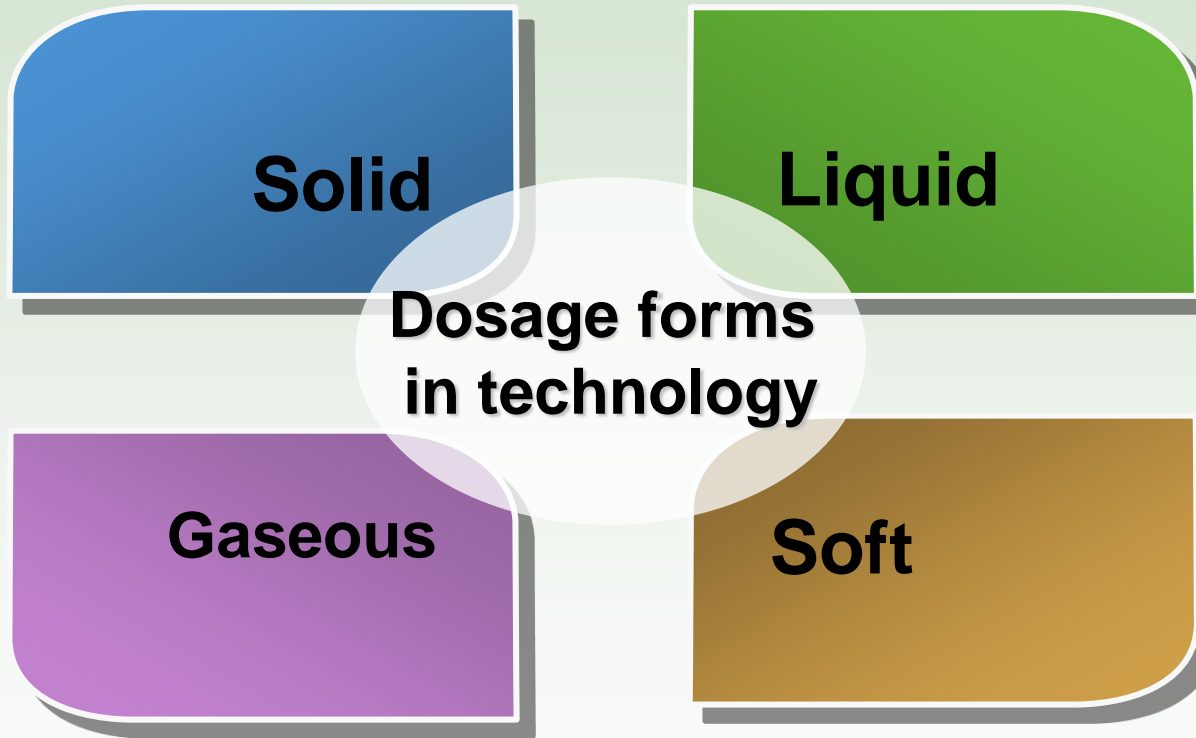


**Dosage
form**



**It is rational in terms of
pharmacotherapy, easy to use and
storage form used
for drug delivery to the patient**

TYPE OF MEDICINAL FORM **AND THE WAY OF ITS ADMINISTRATION**



TYPE OF MEDICINAL FORM **AND THE WAY OF ITS ADMINISTRATION**

Establishing a significant impact of drug forms on therapeutic efficiency and the development of pharmaceutical science contributed to the emergence in the late XX century, a variety of new drug forms

Tablets

Multilayer

Retard

Skeletal

Sublingual

For implantation

For dissolve

Effervescent

**Inhalation aerosols,
foam, film
forming, etc.**

Ocular drug film

**Suppositories
multilayer**

Rektiols

**Eye drops
tube-feed**

**Therapeutic
Systems**

**Sustained
release**

**Controlled
release**

**With targeted
delivery**

TYPE OF MEDICINAL FORM **AND THE WAY OF ITS ADMINISTRATION**

The choice of medicinal form at the same time determines the route of administration of the drug in the body

Ways of drug administration

Enteral

- **Oral**
- **Sublingual**
- **Rectal**
- **Buccal etc.**

Parenteral

INJECTION

- **Intravenous**
- **Intra-arterial**
- **Intramuscular**
- **Subdermal, etc.**

OTHER

- **Inhalation**
- **Transdermal**
- **Instillyatsionny**
- **Intranasal etc.**

TYPE OF MEDICINAL FORM AND THE WAY OF ITS ADMINISTRATION

*The most **common**, most **physiological** and most **convenient** route of administration way is oral*

**70-80% of the drugs that are available
are intended for oral administration**

**In general practice
the most popular
tablets - 50%**

**In pediatric practice
up to 70% are liquid
medicines**

TYPE OF MEDICINAL FORM AND THE WAY OF ITS ADMINISTRATION

According to the degree of release and, accordingly, the bioavailability of oral drugs can be arranged in the following series:

Solutions → Emulsion → Suspensions → Powders → Capsules → Tablets

When choosing the type of medicinal form for oral administration consider the physicochemical properties of the drug, bioavailability and wishes of patients

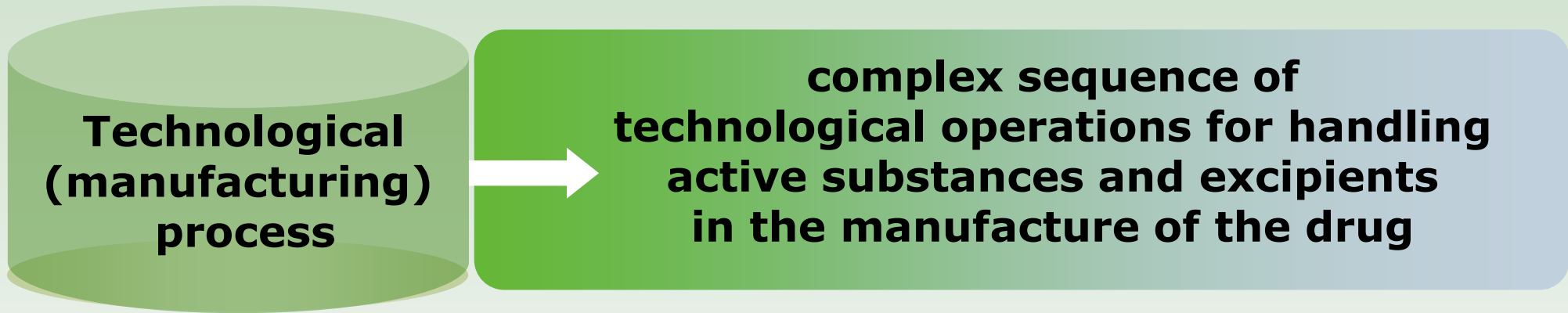
In many cases for oral administration several different drug forms of the same drug are produced (tablets, capsules, syrups, granules, etc.)

TYPE OF MEDICINAL FORM AND THE WAY OF ITS ADMINISTRATION

When introducing drug into the body in different ways and in different formulations the **pharmacological action** direction is preserved, but the **speed** of the therapeutic effect, the **time** and the **strength** of the therapeutic effect may differ significantly

Dosage form and the way of its administration into the body must be clearly substantiated in each case: be comfortable to use, provide maximum therapeutic effect and minimum possible side effects

TECHNOLOGICAL PROCESS



The technological process of medicinal form preparation, consists of several sequential stages of production (granulation, packaging), each includes a number of successive technological operations (weighing, grinding, mixing, etc.)

TECHNOLOGICAL PROCESS

Depending on the physical, chemical, mechanical and other characteristics of the medicinal forms and the properties of drugs and auxiliary substances in the preparation of drugs employ different manufacturing operations and equipment

For example:

Preparation of suppositories

- grinding AS
- preparation of the base
- AS mixing with the base
- pouring suppositories
- packing

Preparation of tablets

- grinding
- mixing
- granulation
- pressing
- packing

Equipment: Ovens, crushers, mills, screens, reactors, tablet machines, mortars, packaging machinery and other.

TECHNOLOGICAL PROCESS

Conditions of the implementation of any technological operation can affect therapeutic effectiveness of drugs that must be considered in the development of their technology

Biological availability of medicinal substance depends:

Changes in conditions or equipment during grinding can cause to change dispersion drug degree

Carrying out moist granulation can cause crystallization and formation another polymorph modification of the drug

TECHNOLOGICAL PROCESS

While drugs are produced all technological operations shall be conducted in full accordance with the approved technology

**NB! Changes in the drug, which can occur with non-adherence to process operations, often can not be established by conventional methods of analysis.
The drug can fully meet current requirements, but do not provide the necessary therapeutic effect**

Strict compliance with the approved modes of technological operations require the GMP principles

TECHNOLOGICAL PROCESS

**"The quality of drugs should be predetermined the principles of GMP"(excerpt from the EU 89/341/EES).
In Ukraine there is guide 42-01-2001 "Drugs.
Good manufacturing practice"**

GMP – Good Manufacturing Practice
**Good manufacturing practices: a set of rules for the
organization of production and quality control**

TECHNOLOGICAL PROCESS

GMP includes a detailed description of all the requirements of the conditions of production of drugs, provides accurate performance of these requirements and establishes the order of strict control over production.

In GMP maximum account and clearly defined the factors that affect the drug quality: buildings and facilities, staff, equipment, organization and implementation process, documentation, control of the production process, quality control of finished products, etc.

TECHNOLOGICAL PROCESS

GPP – Good Pharmaceutical Practice

Special attention is required observance of technology in the manufacture of of drugs in pharmacies on individual prescriptions, when an important role is played by the subjective factors



**Selection
technological
operations and
methods
in pharmacy
depends on :**

Qualification and specialist knowledge

Experience of the person

Analytical mind

Equipment, etc.

PHARMACEUTICAL FACTORS

- Physical state of drugs
- Simple chemical modification of drugs
- Auxiliary substances
- Type of medicinal form and the way of its administration
- Technological process

**Pharmaceutical factors -
it is a tool in the hands of a professional,
through which he provides manufacturing
of high quality and effective drug: easy to use,
with high therapeutic effectiveness
and minimal side effects**

Conclusions:

- Factors - forces acting simultaneously, states or other circumstances that affect the final result of the investigated processes, data or parameters.
- All pharmaceutical factors, which influence on biological effects of drugs, can be divided on 5 groups:
 1. Physical state of the medicinal substance.
 2. Chemical nature of the medicinal substance
 3. Auxiliary substances.
 4. Type of the medicinal form and the ways of introduction it in the organism.
 5. Technological operations, which take place in getting a drug.
- Pharmaceutical factors play an important role in working out the composition and the technology of new drugs and improving already existed.
- In practice of pharmacist-technologist the most important factors are: physical state of the medicinal substance, availability of helping compounds and their nature. Consequently, right choices of the technology of drugs, mechanization of technological process's levels are needed. Pharmacist in drug-store chooses neither medicinal substances nor medicinal forms, because determined form of prescription already exists. There a doctor gives instructions about what medicinal substance must be used and what medicinal form must be prepared.



***THANK YOU FOR
YOUR ATTENTION!***