Ministry of Health of the Russian Federation Volgograd State Medical University

Department of Pharmaceutical and Toxicological Chemistry

# GENERAL PHARMACEUTICAL CHEMISTRY

# CHEMICAL METHODS OF PHARMACOPOEIAL ANALYSIS - IDENTIFICATION OF DRUGS OF ORGANIC NATURE (IDENTIFICATION OF FUNCTIONAL GROUPS) (Identification of the hydroxyl group. Identification of aldehyde and ketogroups)

Lesson 5

V term

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Medicinal products of organic origin constitute the majority of medicinal products. The analysis of these pharmaceutical substances is mainly confined to the examination of the functional groups that make up the compound.

A functional group is a reactive atom or group of atoms that determines the chemical properties of a substance, its pharmacological activity and its belonging to a certain class of organic compounds.

The analysis of drugs by functional groups makes it possible

- to unify the methods of identification and quantification reactions;
- $\succ$  to predict test methods according to their structure.

Medicinal substances are usually polyfunctional compounds, i.e. they contain several functional groups.

In the identification, reactions are usually conducted for all functional groups, which makes it possible to correctly identify the drug substance.

For each functional group several methods of quantification are proposed, which makes it possible to select the optimal method of analysis in the study of medicinal substances in different objects (substance, medicinal product).

# Hydroxyl group identification

## **Identification of monobasic alcohols**

# **1.** Monobasic alcohols can be detected by the esterification reaction or by acetylation with using acetic anhydride:

The reactions are carried out in the presence of water-removing agents under heating.



The esters derived from low molecular weight alcohols have a characteristic odour and the esters derived from high molecular weight alcohols are crystalline substances, and have a distinct melting point.

**2. Oxidation reactions.** Oxidised only by strong oxidants ( $K_2Cr_2O_7$ ,  $KMnO_4$ ,  $HIO_4$ ,  $KIO_4$ ) in an acidic medium. The mechanism of the oxidation reaction is different, depending on the nature of the hydroxyl. For example, ethanol is oxidised to acetaldehyde by potassium dichromate in the presence of sulphuric acid, which is detectable by smell:

$$3 CH_{3}CH_{2}OH + K_{2}Cr_{2}O_{7} + 4 H_{2}SO_{4} \xrightarrow{t}$$

$$3 H_{3}C \xrightarrow{0} + Cr_{2}(SO_{4})_{3} + K_{2}SO_{4} + 7 H_{2}O_{4}$$

Secondary alcohols under these conditions give ketones. Tertiary alcohols oxidise difficultly, breaking the hydrocarbon chain.

# Identification of polybasic alcohols

## **Reactions of complex compound formation.**

The strength of the acidic properties is affected by the number of hydroxyl groups in the compound: as the number of groups increases, the acidic properties increase. Due to this, polybasic alcohols are capable of forming intracomplex (chelate) compounds with metal salts (copper, cobalt) in strongly alkaline media. The reaction with copper (II) sulphate in sodium hydroxide medium is of most interest.



**IDENTIFICATION OF PHENOLS** 



Chemically, the phenolic hydroxyl is generally more acidic than the alcoholic hydroxyl. In addition, the hydroxyl group contributes to The hydroxyl group also increases the electron density of the aromatic cycle and promotes electrophilic hydrogen substitution reactions.

# 1. Complexation reaction with iron(III) ions.

Depending on the number of phenolic hydroxyls, the presence of other functional groups in the phenol molecule, their relative positions, the pH value of the medium and the temperature compounds are formed, with the exception of thymol, that can be colourful and compounded in various combinations.

For example, phenol gives blue colouring, resorcinol gives blue-violet

colouring, salicylic acid gives blue-violet or red-violet colouring, sodium para-aminosalicylate gives red-violet colouring, quinosol bluish-green.



#### 2. Halogenation reactions(bromination and iodination)

Thereaction results in a white precipitate and discolour ation of the bromine water.



# **3. Azocoupling (formation of anazodye)**

Phenols having an unsubstituted para- or ortho-position are easily combined with diazo compounds to form azo dyes. If both ortho- and parapositions are free in the phenol molecule, then substitution occurs mainly along the para-position. When mixing a solution of diazonium salt with an alkaline solution of phenol, an intensely colored precipitate falls out.



## **ALDEHYDE AND KETOGROUP IDENTIFICATION REACTIONS**



#### 1. Formation of Schiff bases.

Aldehydes, condensing with primary amines, form yellow, red or orange- colored Schiff bases:

$$\mathbf{R'} \xrightarrow{\mathbf{O}}_{\mathbf{H}} + \mathbf{H}_{2}\mathbf{N} - \mathbf{R''} \xrightarrow{\mathbf{N}}_{\mathbf{H}} \mathbf{R''} \xrightarrow{\mathbf{O}}_{\mathbf{H}} \mathbf{R''} + \mathbf{H}_{2}\mathbf{O}$$

#### 2. Formation of oximes and hydrazones.

Carbonyl compounds are capable of forming oximes (when interacting with hydroxylamine), and also react with hydrazine derivatives, forming semicarbazones(withsemicarbazide), phenylhydrazones(withphenylhydrazine, etc.).



Hydrazones and oximes are white or colored water—insoluble compounds with a stable melting point.

#### **3. Oxidation reactions of the aldehydegroup.**

1) <u>Thereactionofthe"silvermirror"withanammoniasolutionofsilvernitrate:</u>

$$R \xrightarrow{O}_{H} + 2[Ag(NH_3)_2]NO_3 + H2O \xrightarrow{R}_{O} + 2Ag \downarrow + 2NH_4NO_3 + NH_3^{\dagger}$$

Whenheatedinawaterbathwithatemperatureof50-60°C. Amirror precipitate of metallic silver is formed on the inner walls of the test tube.

2) Interaction with the Nessler reagent in analkaline medium: Agrayish-black precipitate of metallic mercury is released.

$$R - \left\langle \stackrel{O}{\underset{H}{\longrightarrow}} + K_{2}[Hg]_{4}] + 3KOH \longrightarrow R - \left\langle \stackrel{O}{\underset{OK}{\longrightarrow}} + Hg \right| + 4KI + 2H2O$$

3) Interaction with the Fehling reagent. In an alkaline medium, when heated in the presence of aldehydes, a red precipitate of copper (I) oxide is formed.



