

Semester II.

Pharmacology

Laboratory 3 and 4

CHIMOTERAPEUTICS AND SULFONAMIDES

3/4.

Chemotherapeutics & Sulfonamides

- 1. Pharmacognosis**
- 2. Pharmacodynamics**
- 3. Laboratory**
- 4. Pharmaceutical technique**
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2. Pharmacodynamics

Side effects of acaprin

Acaprin is a chemotherapeutic with a quinoline structure used in the treatment of babesiosis in pets. It is presented as a 5% solution in 6ml vials. The treatment is not without risks due to the side effects of the substance.

In order to demonstrate the side effects, symptoms are discussed: the cholinergic effect of the substance: mild myosis, sialorrhea, change of heart and respiratory rate, increased peristalsis, fecal and urine emissions, contraction of the masseteric muscles with noise products of clashing teeth, restless facies, generalized muscle tremors. Symptoms disappear by atropine inj.

3. Lab

Identification of sulfamides

Qualitative identifications

A simple qualitative method is Osadcenko's method. It consists of placing the tablet or powder on a sheet of white paper, porous (blotting paper), after which a drop of concentrated HCl is added. From the resulting combination of conc. HCl, lignin and sulfamide, an intense orange coloration appears.

To identify sulfamides, dissolve 5cg substance in 2ml, 0.1N NaOH, add 10ml distilled water and then, add 2-3 drops of 5% copper sulphate solution.

For sulfathiazole: gray-gray precipitate appears.

For sulfadiazine: green-brown precipitate which then passes to gray-purple.

For sulfadimidine: a green-brown precipitate which then passes to red-brown.

For sulfafurazole (neoxazole) a green coloration, after which, a blue-green precipitate appears.

Sulfathiazole can be distinguished by heating (5 cg substance) until melted.

The substance is reddish-brown and gives off an odor of ammonia, aniline and hydrogen sulfide, which is sulfathiazole characteristic only .

Quantitative identification

There are a number of methods for dosing sulfamides.

Of these, the **amine diazotation** method (or Marshall method) is the most used for determining sulfamide, especially in biological environments. The principle consists in the diazotization with nitrite, in acidic solution, of the aromatic amino group from the para position of the sulfamide and then coupling this product called diazonium, with an aromatic amine. Thus, an azo dye is obtained whose concentration is determined colorimetrically.

The method has a sensitivity 1/1,000,000, but has the disadvantage that it is applicable only to free amine sulfamides (few sulfamides have occupied amine function: prontosyl, formo-sulfamide, phthalyl-sulfathiazole, succinyl-sulfathiazole) no longer used, or because they are not absorbed, have strictly local use in intestinal disorders.

More important is that this method does not dose acetylated sulfamide (the form of metabolism of sulfamides in the body), which has the amine function blocked by the acetyl radical.

The acetylated sulfamide in the body is pharmacodynamically inactivated, so dosing is not important. If, however, we want to dose the total sulfamide from a biological medium (so that includes the acetylated one), we will have to produce hydrolysis in acidic environment, breaking the acetyl radical from the amine function.

Another mention that can be made is that a number of other aromatic compounds that have a free amine function, react to this method (procaine, rivanol or after antifebrin and fanacetine hydrolysis).

Working technique

A therapeutic dose of oral sulfamide is administered to an animal. After 2 hours blood is gathered, on a drop of heparin, 2-5ml of blood. Take 1 ml of this blood and haemolysate with 9ml distilled water in a tube. After haemolysis, add 5ml of 10% trichloroacetic acid to the solution, for proteins' defecation. It is then filtered in another tube, obtaining a clear colorless liquid.

5 ml of this filtrate are taken and passed into another tube. It is treated with 1 ml soil. 0.1% sodium nitrite for diazotation.

Leave one minute, then add 1ml of 0.5% ammonium sulfamate, to neutralize excess nitrite. After 3 min., treat with 1ml of alfa-naftilamine and a coloration ranging from pink to deep red depending on the amount of sulfamide appears. Based on standard curves, it is read on photocolormeter, determining the exact amount of sulfamide found.

4. Pharmaceutical technique

Preparation of the sulfathiazole solution

The solubilization of sulfamides can be achieved only at a strong acid or alkaline pH. For this reason sulfathiazole solutions are prepared by addition of NaOH. 1g of sulfathiazole powder together with 3ml of water and 1ml of 16% NaOH in a tube. Shake until the total solubility is achieved a solution of 20% sulfathiazole being obtained. We measure pH of the solution, finding that it is around 10, indicating alkalinity.

There is discussion on how to administer the sulphathiazole solution, linked to its alkalinity. Thus, S.C. pathway is totally contraindicated, producing necrosis, phlegmons, abscesses. I.M. administration is done only to certain species (e.g. pig), otherwise this pathway being contraindicated, for the usual therapy. In contrast, the solution is administered very well by I.V., where by dilution, and the action of buffer system, the substance cannot produce any adverse effect. However, it will be insisted that the administration be done strictly I.V. since by per venous penetration it gives periflebitis. It is also noted that i.v administration of sulfathiazole in dogs has a central vomiting effect.

Preparation of the sulfamidated haemopansament

In the wounds treatment, sulphamidated hemopansament has particularly favorable effects, the better the wounds are fresh. They combine the bacteriostatic action of sulfamide, with of blood biogenic stimulants, ensuring rapid healing, without keloidal vices.

Hemosulfamidate is a mixture of equal parts of blood and sulfathiazole 20%. It is prepared by collecting blood from the jugular from the animal, which is mixed in a sterile tray, with an equal amount of 20% sulfathiazole solution. In this mixture, the blood does not coagulate. It is left 10 min. in the air, after which it is applied to the wound either as a dressing, which is soaked with sulfamidated blood.

Powdered sulfamidated dressing can also be prepared. The preparation technique is the same as the mixture of blood and sulfathiazole spread on glass plates, allowing them to dry, after which they are scraped with a scalpel and sprayed. In this form the powder can be kept longer and is used in vaginal conditions such as vaginitis.

Preparation of the sulfamidated ointment

The sulfamidated ointment is prepared 10%. Weigh 2g of sulfamide and 18g of petroleum jelly. The sulfamide is mixed in the mortar with a small amount of petroleum jelly, and the rest of the excipient, gradually added until it is exhausted and mix until its homogenization.

The identification of the sulfamidated ointment is done in the same way as has been shown, according to the Osadacenko technique. Thus on a porous strip a small amount of sulfamidated ointment is spread over which 1-2 drops of concentrated hydrochloric acid are added. The orange color appears. If we do the same thing with a zinc-coated ointment, hydrochloric acid, an ash-gray slurry, appears on the periphery of the area

Preparation of a 1‰ rivanol solution

Weigh 0.2g rivanol and add 100ml distilled water, stirring until dissolved. The rest of the water is filled up to 200ml, after which it is filtered. We will take care that the preparation is not carried out with physiological serum, as NaCl precipitates rivanol by modifying its electrostatic state.

Rivanol solution 1‰ is used externally as a wash on mucous membranes, or it can be injected intravenously in some microbial conditions.

Preparation of a 3% tripaflavin ointment

Weigh 0.3g tripaflavin and dissolve in little water, then add 10g, simple ointment (1:1 petroleum jelly: lanolin). Gradually mix until homogenized.

Tripaflavin ointment is used in disorders of vaginal and preputial mucosa, trichomonosis, to protect the hands in gynecological and obstetric interventions in animals.

Preparation of pioctanine solutions

Pioctanine is prepared in 1% aqueous solution or 1% alcoholic solution. The preparation is done according to the usual techniques in making solutions.

Pioctanin solutions are used with very good results in dermatomycosis, wet exemas, horse mumps, various exudative dermatitis.

5. Pharmacography

Rp./

Compr. Arsevin 0.25
D.t.d. XVI
S. int. 2 x 1/zi
To calf with enteritis

Rp/

Tripaflavin 1.5
Vaseline ad 50.0
M.f. ung.
D.S ext
in vaginitis

Rp/

Pioctanin 1.0
Aq. Distill. ad. 100.0
M.f. sol.
D.S. ext. s.c. inj. in horse foot inflammation

Rp/

Compr. Sulfathiazol 0.5
D. t.d. Nr. LVII
S. int. after indication to sheep

Rp./

Neosalvarsan 4.5
D.t.d VI.
S. Ext. în inj i.v. to horse 2 x1/day dissolved in 100ml
distiled water

Rp./

Rivanol 1,0
Aq. Distill q.s. ad. 1000,0
M.f. sol.
D.S. ext. in vaginal wash

Rp./

Acaprin 5% of 6 ml vials II
D.S. int. s.c. inj. In babesiosis to cow

Rp./

Albastru of methylene 0.5
Aq. Distill. q.s. ad 50.0
M.f. sol.
D.S. ext. i.v to cow, inj. in cyanogenetic intoxication

6. Classification

Chimiotherapeutics		
Group	Subgroup	Representative
Arsene		<i>Neosalvarsan; Spirotripan; Atoxil; Stovarsol</i>
Stibium		<i>Antimosan; Neoantimosan; Fuadin; Stibosan; Neostibosan</i>
Acridine		<i>Tripaflavin; Rivanol; Entozoon; Atebrine; Bovoflavine</i>
Dyers	Oxyquinoleine	<i>Acaprin; Saprosan; Iodisept; Cifoform; Chinosol</i>
	Triazines	<i>Berenil</i>
	Benzidine	<i>Tripan blue; Naganol;</i>
	Trifenilmethane	<i>Pioctanine</i>
	Thiazinic	<i>Methilene blue</i>
	Quinalidinic	<i>Antricide sulphate</i>
	Nitrofuranic	<i>Nitrofurane; Manis; Furazolidone; Galifurane</i>
	Nitrothiazolic	<i>Lavoflagin</i>
Others		<i>Amprolium; Nicarbazin; Dimetridazole; Negram; Osmatin</i>

Sulphonamides

Sulphonamides		
Group	Subgroup	Representatives
Sulphonamid	Potentiators	<i>Diaveridin; Pirimetamin; Trimetoprim</i>
Sulphonamids	General-action	<i>Sulfanilamida; Sulfacetamida; Sulfatiazolul; Sulfadimidine; Sulfachinoxaline; Sulfacoccidin; Sulfanilureea; Trisulfamide</i>
	Local-action	<i>Ftalisulphathiasol; Formosulphamide; Sulfoguanidin; Succinilsulphathiazole</i>
	Renal	<i>Neoxazole</i>
	Semi-retarded	<i>Sulphaphenasole; Salphadiazine; Sulphamerasine; Sulphametoxasole</i>
	Retarded	<i>Sulfametin; Madribon; Retamid</i>
	Ultra-retarded	<i>Sulphormethoxin; Sulphametoxipirazine</i>
	Sulfamide assoc. with potentiators	<i>Borgal; Tribriksen; Trivetrin; Sulfotrim; Formetoguard; Sulfaveridine</i>
	Hemosulphonamids	<i>Marfanil</i>
Suphones		<i>Diasona</i>