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 Résumé
 

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STUDIES ON THE ANTIMICROBIAL  
ACTIVITY OF SULFADIMETHOXINE  
AND ITS RELATED COMPOUNDS. III  
ON SULFADIMETHOXINE  
CONTENT IN RABBIT PLASMA  
IN RELATION TO ITS  
ANTIMICROBIAL ACTIVITY  
IN VIVO

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The authors showed that antimicrobial activity of sulfadimethoxine was more or less significantly antagonized by peptone, beef extract, horse serum and  $\rho$ -aminobenzoic acid in the same grade with other sulfas.

We also confirmed that sulfadimethoxine combined with rabbit plasma protein *in vitro* in the similar fashion as other sulfas.

The concentration of sulfadimethoxine in plasma was measured by several methods to show different values, for the estimation of an active form of sulfadimethoxine in blood, biological methods seem superior to chemical ones.

The combination of this sulfa with rabbit plasma protein is considered to occur immediately after it is brought into blood stream, in view of the fact that the combining ratio was as high as 90%, independent of times after administration. It was also shown that plasma combined sulfadimethoxine was decomposed to the free form in the presence of homogenized rabbit kidney.

STUDIES ON THE ANTIMICROBIAL  
ACTIVITY OF SULFADIMETHOXINE  
AND ITS RELATED  
COMPOUNDS. IV  
ON THE PRODUCTION OF  
RESISTANCE

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Sulfadimethoxine was examined as to the production of drug resistance of pathogenic bacteria and also cross resistance in comparison with sulfamethoxy pyridazine and sulfisoxazole.

The test organisms, *Staphylococcus aureus*, *Escherichia coli* and *Shigella flexneri*, proved to acquire drug resistance to sulfadimethoxine in considerably high and almost same degree as to the other two sulfas by transferring those each culture into broth containing one-half of its inhibiting concentration of the drug.

Cross resistance was also recognized among those resistant strains obtained and the three sulfas in almost complete grade.

Thus it may be concluded that sulfadimethoxine as one of long-lasting sulfas seems to have the same properties as the other sulfas in drug resistance.

STUDIES ON THE ANTIMICROBIAL  
ACTIVITY OF SULFADIMETHOXINE  
AND ITS RELATED  
COMPOUNDS. V

FUNDAMENTAL STUDIES ON  
SENSITIVITY TEST OF BACTERIA  
BY MEANS OF TEST PREPARATION  
OF LONG-ACTING SULFA DISK  
USING SULFADIMETHOXINE

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In an attempt to apply disk method for sensitivity test of pathogenic bacteria isolated from clinical materials to long-acting sulfas, sulfadimethoxine disks and also sulfisoxazole disks as control were prepared by the authors and were tested as to 38 strains of gram-positive and gram-negative bacteria in a comparison with agar-dilution method. The results obtained were as follows:

1. Dilution method showed that the test organisms had, in general, similar sensitivity to the two sulfas but the grade was more or less significantly different each other in the strains.

2. In disk method, sensitivity of the organisms was also almost same between the two kinds of disks and its difference in the strains was not so conspicuous as in the former method.

3. Statistical analysis shows that correlation between sensitivities of the organisms by agar-dilution and disk methods was estimated as significant and that a linear relationship existed between the minimum inhibitory concentrations of the sulfas' disks and diameters of their inhibition zones.

Thus it is concluded that sensitivity test by long-acting sulfa disks may be valuable in practical use.

### STUDIES ON ANTIMICROBIAL ACTIVITY OF CHLOROHEXIDINE

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The authors studied on the antimicrobial activity of chlorohexidine (1, 6-di-(N<sup>4</sup>-p-chlorophenyl-N'-diguano)hexane), and the following results were obtained.

1. The compound was confirmed to have strong bacteriostatic and bactericidal actions on various kinds of pathogenic microorganisms including fungi. This bacteriostatic action is not antagonized with peptone, beef extract and p-aminobenzoic acid but with beef serum, and the bactericidal action is antagonized with dried yeasts.

2. The bacteriostatic action was significantly antagonized with beef serum, but not with peptone, beef extract and p-aminobenzoic acid, and the bactericidal action was antagonized, to same extent, with dried yeasts so far as their concentration used were concerned.

3. Drug resistance to the compound developed only in low degree as a result of long serial passage *in vitro* as to each one strain of *Staphylococcus aureus*, *Escherichia coli*, *Shigella flexneri* 2a and

*Salmonella typhi*.

4. The compound significantly inhibited the acquisition of resistance of *Shigella flexneri* 2a (the same strain as in 3. was used) to dihydrostreptomycin and sulfadimethoxine by its addition *in vitro*.

5. In view of the above results, the compound may be regarded as a very excellent bactericidal agent.

### STUDIES ON THE *IN VITRO* BACTERIOSTATIC EFFECTS OF LEUCOMYCIN, ESPECIALLY ABOUT A<sub>1</sub> FRACTION

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Leucomycin, an antibiotic found by HATA *et al.* was studied its bacteriostatic effects *in vitro*, especially about the A<sub>1</sub> fraction purified by means of counter-current method in comparison with erythromycin and some other antibiotics. The results obtained were as follows:

The A<sub>1</sub> fraction proved to have the similar antibacterial spectrum with leucomycin base, erythromycin and oleandomycin, the last being the weakest in bacteriostasis among these antibiotics and the A<sub>1</sub> fraction somewhat stronger than the base.

It is to be noted that the A<sub>1</sub> fraction showed stronger bacteriostatic action against some antibiotic-resistant strains of *Staphylococci* as well as the sensitive ones than the other tested antibiotics, namely, leucomycin base, erythromycin, oleandomycin, penicillin and chloramphenicol. And the bacteriostatic action of the fraction was not affected by the change of pH and the addition of blood and its components.

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