

STUDY GUIDE 2: SYNTHETIC ANTIBACTERIALS: THE SULFONAMIDES:

1. Why are sulfonamide antibacterials acidic? Why are sulfonamides such as sulfisoxazole more acidic than sulfacetamide or sulfanilamide? Understand the relationship between resonance and acidity and be able to apply it relative acidity.
2. Why does the water solubility of the sulfonamides decrease as pH decreases as indicated in Table 1? DON'T MEMORIZE this table, just understand it.
3. What factors determine water solubility/lipophilicity
4. Do not memorize the drug structures shown in the chapter. You will not be asked to recall these from memory (see 24 below).
5. What bacterial enzyme does the sulfonamides inhibit to produce its chemotherapeutic effect? Why are they capable of inhibiting this enzyme? Specifically, how does this result in decreased bacterial DNA synthesis? Is this a static or cidal action?
6. What role does ionization and pKa play in mechanism of action and entry in target bacteria?
8. YOU NEED NOT MEMORIZE the folate biosynthetic scheme, but if given the structures of PABA and the DPAD precursor, you should be able to draw the structure of the DIHYDRO-PTEROATE product.
7. Why are the sulfonamides selectively toxic to bacterial cells versus mammalian cells (Selectivity)?
8. How and why do sulfonamides function as pseudo-substrates?
9. What are the known mechanisms of resistance to the sulfonamides? What is the MAJOR mechanism and how is it transferred to other bacteria? Which other antibacterial drug are sulfonamide-resistant bacteria resistant to and why?
10. What gram positive and gram negative bacteria are the sulfonamides effective against. DON'T MEMORIZE TABLE 2. This is just for you information.
11. What forms (free acids or salts) of sulfonamides are administered orally? Parenterally?
12. What is the primary site and mechanism of absorption for orally administered sulfonamides?
13. What is the relationship between sulfonamide lipid solubility, pKa and plasma protein binding? Why are the sulfonamides widely distributed?
14. Do the sulfonamides cross placental membranes? Enter the CSF? Are they excreted in milk?

15. What is the primary inactive metabolite formed from most sulfonamides (be able to draw this metabolite given a parent sulfonamide)?
16. What is the major route (renal, biliary) and mechanism(s) of excretion for the sulfonamides and metabolites?
17. Why do some sulfonamides produce crystalluria? List three ways this problem be corrected or avoided?
18. What is the relationship between sulfonamide lipophilicity, plasma protein binding and duration of action?
19. Should sulfonamide doses be adjusted in renally impaired patients? Why?
20. What the major sulfonamide prodrugs? What enzymes are responsible for conversion of these prodrugs to their active forms? Why are these prodrug forms effective in the treatment of GI tract infections?
21. Which sulfonamides are used in ophthalmic preparations? Which are used for burn therapy.
22. Why is mafenide acetate not a "true sulfonamide"? Why does this agent produce acidosis when it distributes systemically?
23. What are the two major GENERAL pharmacokinetic drug interactions observed with the sulfonamides. Be sure you understand the mechanism of these interactions?
24. **YOU WILL NOT BE REQUIRED TO IDENTIFY SPECIFIC SULFONAMIDE DRUG STRUCTURES FROM MEMORY!** (For example, I will not put the structure of sulfisoxazole on the exam and ask you to identify it from memory). This holds true for the ENTIRE COURSE.
25. **YOU WILL NOT BE REQUIRED TO LEARN TRADE NAMES FOR THIS COURSE** (They are included in the Lecture Guide for your information and convenience).