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第八章 第三节 强心苷类化合物

Chapter 8，Section 3 Cardiac Glycosides

Oral text 授课口语稿

（授课 20 分钟内）

Slide 1: Next, we will learn the section two of Chapter 8, the "Cardiac glycosides" which is a very unique sort of constituents in TCM. I said it is unique with two point meaning: one point: they are with very unique structures and the other: they are with very strong cardiac effects.

Slide 2: After this section study, we are required to "**To master The types and structure feature of cardiac glycosides"** That means when you see the structure, you can tell it is cardiac glycoside and also you know it is which kind of cardiac glycoside, the detail type. Also we are required to "**To be familiar with The relationship between structure and efficacy"** and to know **"The chemical compositions in TCM *Digitalis lanata* and *D. purpurea"*** which is the common TCM containing the cardiac glycosides.

Slide 3: Glossary

Slide 4: Before learn Chemistry, do you know **Cardiac Failure.**

Cardiac failure can be described as the inability of the heart to pump blood effectively at a rate that meets the needs of the metabolizing tissues. This occurs when the muscles that perform contraction and force the blood out of heart are performing weakly. Thus cardiac failures primarily arise from the reduced contractility of heart muscles, especially the ventricles. Reduced contraction of heart leads to reduced heart output but new blood keeps coming in resulting in the increase in heart blood volume. The heart feels congested. Hence the term congestive heart failure.

Slide 5: First let's see "What is Cardiac glycosides" Cardiac glycosides are a group of plant constituents used in the treatment of cardiac failure. They are glycosides with sugar residues linked to the C-3-OH groups of the cardiac steroid aglycones.

Slide 6: Then what is **chemical structures and how to class them?**

We can divide cardiac glycosides structure in two parts: aglycone and sugar moietie. (Explain the figure).

Slide 7: The cardiac aglycone is a steroid compounds with an unsaturated lactone ring attached to the C-17 of the steroid backbone. The structural feature is as following:

A unique set of fused ring system that makes the aglycone moiety structurally distinct from the other more common steroid ring systems. Rings A/B and C/D are commonly cis fused while rings B/C are all trans fused.

Slide 8: We can see it more clear from stero structure.

Slide 9: The substituted groups at C-10, C-13 and C-17 positions are all β -conformation. The substituted groups at C-10 position can be methyl or hydroxy methyl, at C-13 is methyl group and at C-17 is definitely an unsaturated lactone ring. There are also many substitutes groups at other position of backbone, Among them there is usually a 3 β hydroxy group via which sugar residues are linked glycosidically to the cardiac steroid aglycones.

Slide 10: The lactone moiety at C-17 position is an important structural feature. The size and degree of unsaturation varies with the source of the glycoside. Normally two classes have been observed in nature cardiac aglycone - the cardenolides(A-type) and the bufadienolides (B-type)(see figure below). The cardenolides have a 5-membered unsaturated lactone ring while the bufadienolides have 6-membered unsaturated lactone ring. And usually plant sources provide a 5-membered unsaturated lactone ring while animal sources give a 6-membered unsaturated lactone ring.

Slide 11: About 20 types of sugar(saccharide) residues were found in cardiac glycosides, most commonly used include L-rhamnose, D-glucose, D-digitoxose, D-digitalose, D-digginose, D-sarmentose, L-vallarose, and D-fructose. These sugars predominantly exist in the cardiac glycosides in the β -conformation.

The types of sugar found in cardiac glycosides can be devided in 3 types: 2,6-dideoxysugar moiety, 6-deoxysugar moiety and normal sugar moiety. The special one is 2,6-dideoxysugar moiety, such as digitoxose which occur only in cardiac glycosides.

Slide 12-13: Usually the sugar chain is attached to the 3 β -OH group. There are one to 5 sugars moieties in the sugar chain in most cardiac glycosides. These sugars predominantly exist in the cardiac glycosides in the β -conformation.

There are 3 sorts of sugar chains:

A type: aglycone-(2,6-dideoxy sugar)x-(D-glucose)y

B type: aglycone-(6-deoxy sugar)x-(D-glucose)y

C type: aglycone- (D-glucose)y

Slide 14: The aglycone part is key to activity. The active intensity is depended on the streo structure of backbone, the type of unsaturated lactone ring and the substitutes attached to the backbone. The sugar moiety has no effect itself but can modified the strength caused by the aglycone.

Slide 15: Usually steroid backbone has rings A/B and C/D in cis fused system while rings B/C are all trans fused system. This will let the "backbone" U shape which is very important to activity. Usually, conversion to C/D ring trans fusion are inactive. Conversion to A/B trans system leads to a marked drop in activity although not mandatory A/B cis fusion is important.

Slide 16: The unsaturated 17-lactone plays an important role in receptor binding. Saturation of the lactone ring, attacheing to C-17 in α -conformation or the ring broken dramatically reduced the biological activity.

Slide 17: Although the sugar moiety is not necessary to activity directively. It appears to be important for the partitioning and kinetics of action. When a sugar residue attached to aglycone, it will inhance the hydrophilic property of molecule, the the toxic will become less.

Therefore, when sugar chain grows longer, although the activity is become weaker, the molecule become more safe since the aglycone partion in the whole molecule become less.

Slide 18: Digitalis lanata is belonged to Scrophularia family. It has been using for hundreds of years on treatment of cardiac failure. The active components in Digitalis lanata are cardiac glycosides, which belong to A-type the cardenolides, the Totally over 30 cardiac glycosides have been found in the leaves of the plant. Among them, the lanatosides A an C are the most rich ones.

Slide 19: In pharmaceutical industry, the cardiac glycosides from Digitalis lanata are as the main source of the drugs cedilanid-D and digoxin.

Slide 20: The Scilla maritima (海葱) and Bufobufo gargarizans (中华大蟾蜍) contain B-type bufadienolides cardiac glycosides.

Slide 21: This is the structures of bufadienolides cardiac glycosides. We can see they contain the 6-membered unsaturated lactone ring. We need to notice that the one in Bufobufo gargarizans is not a glycoside. Why? Because it is come from animal. So the is an amino acid residues replace of the sugar moiety.