

PHARMACOGNOSY AND PHYTOCHEMISTRY

Dr.Galvina Pereira

Department Of Pharmaceutical Science and Technology

Institute Of Chemical Technology Mumbai

Week 5

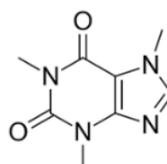
Lecture 21

Introduction to Alkaloids

Hello everyone, and welcome to week 5 of the NPTEL course on pharmacognosy and phytochemistry. This week, we are going to focus on a set of very potent natural compounds: alkaloids. Alkaloids, as the name suggests, are alkali-like compounds found in nature, and their alkaline nature is attributed to the presence of nitrogen. Alkaloids are defined as naturally occurring nitrogen-containing organic compounds found primarily in plants but also in some other organisms, including bacteria, fungi, and some animal species. Because they are alkaline in nature, the nitrogen is mostly in a negative state of oxidation. If consumed, they are intensely bitter, and the majority of them are pharmacologically active. They are a very potent class of compounds compared to other classes of phytoconstituents. Here are some examples of alkaloidal compounds around us.

What are Alkaloids?

- Alkaloids are naturally occurring nitrogen containing organic compounds found in primarily in plants, though some can also be produced by fungi, bacteria, and animals.
- Nitrogen is mostly in the negative state of oxidation.
- Most of them are bitter and pharmacologically active



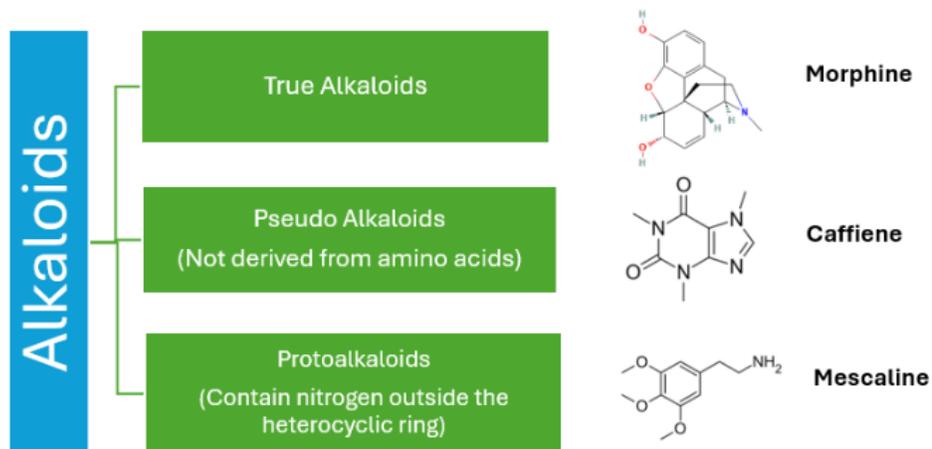
Caffeine

If you look at your beverages, especially tea and coffee, you might have heard of a compound called caffeine. Caffeine, which is present in tea and coffee, is an alkaloid. In chocolates, you will find compounds such as theophylline and theobromine. If you have heard of an antimalarial compound called chloroquine, it is derived from a compound called quinine. Quinine is found in cinchona bark.

Cinchona bark was originally used by the Jesuits to treat malaria. And that's where the genesis of your chloroquine, which is a famous anti-malarial compound is. Now, owing to evolution and owing to more potent drugs, chloroquine is declining in its usage, but still makes up a good role model to study the evolution of your drugs coming from nature. So if you see alkaloids and if you see the clear definition

alkaloids are nitrogen containing heterocyclic compounds and are known to have their genesis from amino acids as a biosynthetic pathway. So when I am talking of alkaloids I could principally divide them into three classes and The first class would be true alkaloids. The true alkaloids are the ones which have both of these factors incorporated in them.

Classification of Alkaloids



That is the nitrogen is a part of heterocyclic ring and secondary in terms of their biosynthesis they are derived from an amino acid biosynthetic pathway. To give you an example of alkaloid which is a true one you can see your morphine. So here it is

morphine. Morphine is given as an analgesic, a painkiller and is also used to make a lot of banned substances.

Now coming to the next compound and that's your pseudo alkaloids. Pseudo alkaloids are slightly different from alkaloids in a way that they have nitrogen as a part of heterocyclic ring. But in terms of their biosynthesis, they are not derived from amino acids. So in that case, you have an example of caffeine. Caffeine generally comes from your xanthine and do not have a clearly what is called as amino acid biosynthetic pathway.

The third case is a case where actually your alkaloid is derived from amino acid. As you can see here, in mescaline, the nitrogen is outside the ring. So here, despite being derived from amino acid, it is no longer a part of heterogeneous ring. Such cases, these alkaloids are called as protoalkaloids. An example of this is muscalin, which occurs in peyote cactus or Sao Pedro cactus.

Now, this cactus species are endemic to Ecuador and Peru and South American countries so during the desert this cactuses store a lot of water as well as alkaloidal substances so people those who consume this cactus while consuming or think once they are thirsty they tend to hallucinate because this has psychedelic effects So mescaline is one example.

Another example is your conicin. So if you see alkaloids, alkaloids are very, very potent class of compounds. They have effect on CNS like caffeine, mescaline or even they have anti-inflammatory, analgesic. In the subsequent lectures, you will see lot of other potent effects of alkaloids. So

Just a brief once again, true have their biosynthesis from amino acid pathway as well as nitrogen in the heterocyclic ring. Pseudo do not have amino acid biosynthetic pathway and proto have their nitrogen outside the heterocyclic ring. Now, what role do the alkaloids play in nature? Alkaloids, being potent, are very defensive and help get rid of herbivores, animals, and insects. I'll give you an example—an interesting one.

So, if you're a Harry Potter fan, you must have heard of the wolfsbane potion, which comes from an alkaloid-containing plant called aconite. Now, aconite roots have been

used as poisons. So much so that they have been applied to arrows to kill animals. At the same time, if you are trekking and come across aconite flowers, if you

just touch them, your hands will turn numb. That is the level of potency this compound has, and we all know the potency of nicotine. Nicotine is present in your tobacco and is known as a CNS stimulant but also if you know the advantages of nicotine has been traditionally used as an insecticide and pesticide because it produces the same effects in insects, but insects do not tolerate it, so it has a lethal effect on them. It also

protects against certain microbes—they are very good antimicrobials. They carry out the process of allelopathy. Allelopathy is a process of mutual suffering where you will see a plant, especially one containing alkaloids, will not allow other plants in its vicinity to grow and flourish. So, this plant will synthesize alkaloids that will leach into the air and soil.

They will reach the next plant. The moment they reach the next plant, what will happen is the next plant will go into some kind of growth. This happens through numerous processes. These growth processes are hampered, and the plant stunts in growth, eventually withering and dying.

So, it has a role to play in plant growth and development. It plays a vital role in repulsion of pollinators or, in some cases, even attraction of pollinators, and it's a good source of nitrogen storage. So, these are the vital functions of alkaloids in plants. Now, if you see the properties of

alkaloids, they are alkali-like, basic in nature. In terms of their molecular properties, they are mostly crystalline, except nicotine, which is liquid. At room temperature, emetine is amorphous, not crystalline. Most alkaloids are colorless, but there are exceptions, such as berberine, which is yellowish, and betanidine, which is slightly reddish in coloration.

Because they are nitrogen-containing, they are mostly basic in nature. But what happens if this nitrogen is surrounded by something? Let's add a little chemistry to this. So, if nitrogen is surrounded by a functional group that is electron-donating, that increases the basicity of your alkaloid.

But imagine if your nitrogen is surrounded by something that is electron-withdrawing. Say, for example, your nitrogen is surrounded by a carbonyl. So in those cases, they tend to be more neutral or acidic. They lose their basicity. So if you see piperine or if you see colchicine, in that case, they won't be basic.

They'll be more neutral compounds because of the electron-withdrawing neighbors that they have next to the nitrogen moiety. Now, most of these alkaloids form water-soluble solids. Now, alkaloids may be present in their native form as nitrogen-containing compounds. But what happens is, owing to their basicity, they attract a lot of acidic compounds and tend to form salts.

Properties of alkaloids



Crystalline solids (Except: Nicotine, emetine etc.)

Colourless (Except: Berberine, betanidin etc.)

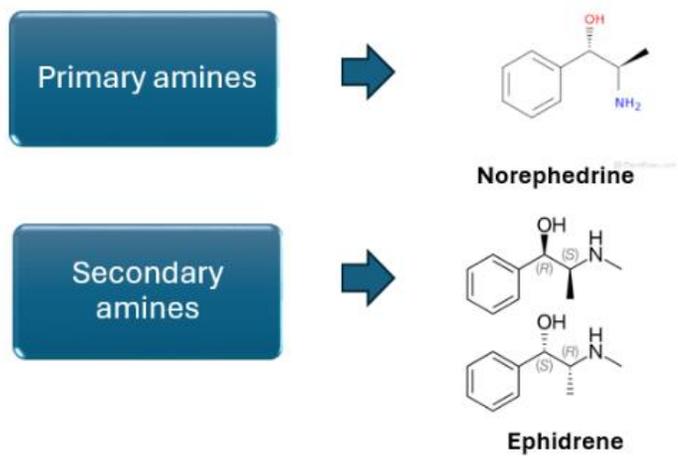
Basic in nature(Except: Colchicine, Piperine)

Form water soluble salts(Except: Quinine sulphate)

Now, they may attract some organic acids, like oxalic acid. Or in some cases, very specific acids such as meconic acid, quinic acid, and so on. So these conjugates occur, and alkaloids tend to form associations with tannic acid. Because they are basic and tannic acid is acidic in nature. So they occur in plants as such, or they might occur in the form of salts.

When they occur in the form of salts, the salts are generally water-soluble. Except in a few cases, take for example quinine sulfate, which is a water-insoluble salt. Now let's see structurally. Now, structurally, there is also a huge difference between the alkaloids. In some alkaloids, the nitrogen occurs or takes the form of a primary amine.

Structures of Some alkaloids



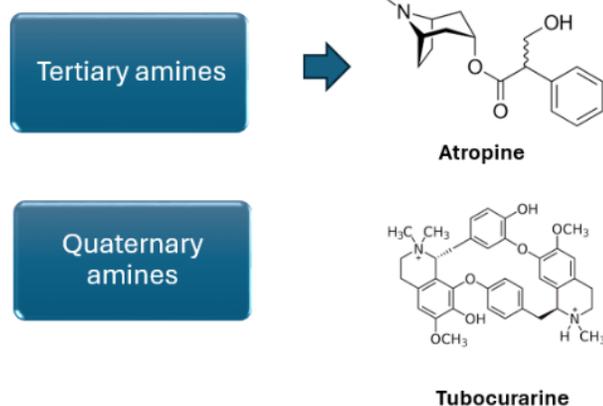
Dr. Galvina Pereira, ICT Mumbai

7

So, if you see here, the norephedrine structure—the alkaloidal nitrogen—it's definitely a proton but acquires a primary amine functionality, whereas if you see ephedrine, Now, what happens in ephedrine is one of the hydrogens gets replaced by a methyl group. So, these are both isomers of ephedrine.

So, in this case, it acquires what is called a secondary amine structure. Now, they might also occur as tertiary amines. Take the case of atropine, which is found in belladonna or *Atropa belladonna*. And this is also present in some cases of local anesthetics, such as tropane. So, you will see a nitrogen here, and the nitrogen here is a tertiary amine structure.

Structures of Some alkaloids



Dr. Galvina Pereira, ICT Mumbai

8

And in some cases, they also have a quaternary character. A good example of such cases is tubocurarin. So, if you see tubocurarin, it forms an association with four atoms in its vicinity. As a result, it acquires a net positive charge, and we call that a quaternary amine. So, alkaloids may occur as primary, secondary, tertiary, or quaternary amines.

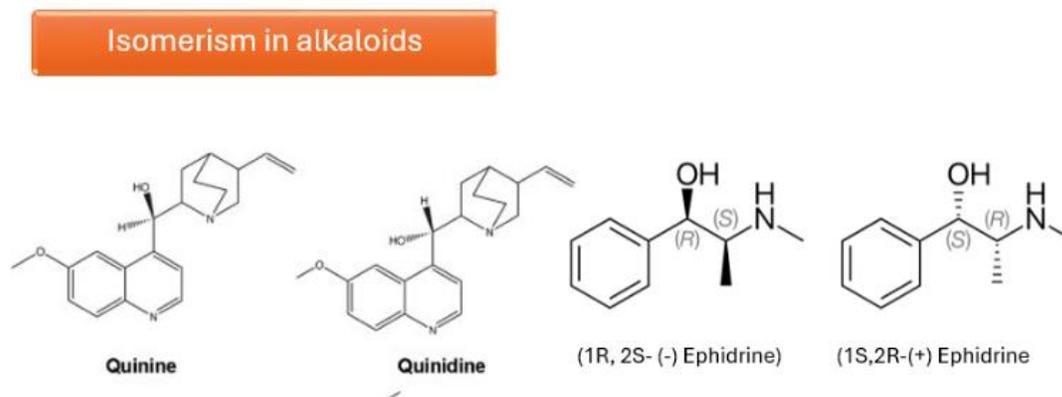
Now alkaloids also occur in different isomers, stereoisomers. I'm just giving or pointing out two examples of isomers and how they affect us. So let's take a case which is this cinchona, which contains quinine. Now if you see cinchona, it does not just contain quinine; it contains numerous other alkaloids. The alkaloids are quinine, quinidine, cinchonine, and cinchonidine.

Just to give you four examples. Now, of these, quinine and quinidine are stereoisomers. So if you see here, they differ in their isomerism principally at the 8th and 9th positions. But I am not putting this hydrogen into perspective. Just see the hydroxyl.

It's different here. And why this difference matters to us is that quinine is a pharmacologically antipyretic molecule. So it helps in malaria. It helps decrease your fever. Whereas if you see quinidine,

quinidine is a molecule that, despite being a stereoisomer, has a much lesser or negligible effect. Activity as antipyretic, but it is more famous as an antiarrhythmic agent. So, it is

used to treat heart disorders such as arrhythmia. The same is the case with ephedrine. If you see the L-isomer of ephedrine,



the L-isomer of ephedrine is almost twice as potent as the D-isomer of ephedrine when it comes to nasal decongestant effects. Now, let's see how you detect alkaloids. Now, alkaloids are nitrogen-containing compounds. We saw that they do not fit into a particular law. When I said basic, there were exceptions.

When I said crystalline, there were exceptions. When I said primary amines, you also saw there are secondary, tertiary, quaternary amines, and so on. So, putting alkaloids in one box is difficult, but there are a few chemical tests that can help us assess if the plant contains alkaloids or not. Now, when you're detecting alkaloids, you're basically detecting a nitrogen group.

Now, in addition to alkaloids, there might be proteins in the plants that could interfere with the detection. So, what is done in this case is we know that proteins are not soluble in alcohol, and that's precisely the step we use. What is done is the plant extract or the plant part is taken and This plant part is basified. The reason being, if you think of a salt or alkaloidal salt, we saw that alkaloidal salt is water soluble.

So let's convert it into a free base and for converting it into free base, you add a little base. So take your extract or take your plant material, convert it into a free base. by adding alkali and then this free base because of its unionized nature has more affinity to organic solvents. So in this case what we can do is rather than extracting it with water which will extract your proteins as well let's extract it with alcohol.

So an alcoholic extract is taken now the alcoholic extract doesn't contain protein and whatever nitrogen is detected is detected chiefly because of alkaloids. Now this alkaloidal nitrogen has a good affinity to form colored complexes or precipitates with iodine. So different salts of iodine are taken. They called as different coloring agents

and their ability to form precipitate with this nitrogen containing compounds form the basis of most of the chemical tests. So the alkaloids or the alcoholic extract of this plant can be reacted with dragondorf reagent which is potassium bismuth iodide. In this case the color complex that we get is a red color precipitate. Or with Mayer's reagent, in this case, what is used is a potassium mercuric iodide.

So you see iodide is a common entity in all of this. will form a pale yellow to whitish precipitate. Hager's reagent is again detecting your amino group, and it's your picric acid. It reacts with amine groups to form a yellow-colored precipitate. One more iodine-containing reagent is your Wagner's reagent, which is iodine and potassium iodide.

This forms a reddish-colored precipitate. Now, let's see a detailed view of all these chemical tests to understand the principle behind them. And once we have done it, you'll be very clear about how alkaloids are extracted and detected. So, look here; what we're taking is a *Solanum xanthocarpum* extract, which contains your solasodine. This extract is slightly orange because



we have taken a fruit extract to which we add your Dragendorff reagent, which is also orange. We should not get an orange coloration; instead, we would get a precipitate. And as you can see, as they react, the orange precipitate is being formed. Similarly, you can take the Solanum extract and add your Mayer's reagent to it. This is your potassium mercuric iodide, and it should give you a slightly pale buff-colored precipitate compared to your Dragendorff.

So on addition of Mayer's reagent, you will see a buff-colored precipitate, but note that since the extract is slightly orangish, you are getting a little orange color. However, overall, the product, when it settles, is buff-colored. Now, the third reagent is your Hager's reagent, which is your picric acid. Again, to the Solanum extract, we will add the Hager's reagent.

With Hager's reagent, it should form a yellow precipitate. So, let's observe. So, it's a solution, and now what you get is a precipitate. So, what we will do is, when we compare the tubes, you should be able to see

that Dragendorff's is more orange, your Mayers should be more buff, and your Hager's reagent should be more yellowish. Just observe the difference between this orange, buff,

and yellow-colored precipitate. So, from these videos, we learn how to evaluate your alkaloids or alkaloid-containing drugs. So, here are a few references if you want to know more about the alkaloids.

And thank you all for your patient listening. Thank you.