

PHARMACOGNOSY AND PHYTOCHEMISTRY

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Week 9

Lecture 45

Resins containing drugs

Hello everyone and welcome to the NPTEL course in pharmacognosy and phytochemistry. We are doing resin containing drugs and in this session we are going to learn about two resins which are used commercially and for recreational purpose and those resin containing drugs are cannabis and guaiacum resin. Now cannabis.

What is cannabis? So cannabis you heard numerous things about cannabis. It's used as a recreational drug. It is good. It is bad.

There are numerous countries wanting to make this drug legal and some say that it is better off illegal because of its what is called as addiction effects. Now here since it's an addicting drug and it's also therapeutically beneficial Let's learn a little bit about this drug and let's try to understand why there is a debate here. Now cannabis basically consists of dried leaves as well as flowering tops of two plants.

Now cannabis has numerous benefits. Species of which two which are used very much for commerce and for recreational purpose are cannabis sativa which is thought to be the main plant and from which other cannabis hybrids or varieties have been prepared and the other one is cannabis indica. Now they belong to the family Cannabinaceae.

Now if you see cannabis, there are numerous type of cultivated varieties or often referred to as cultivars. So what are these cultivars? Now cannabis was known as initially a drug which was used for preparation of fibers. If you see your hemp, You get numerous products in market which are made up of hemp.

Say for example your hemp jeans that is your traditional Levi's jeans was thought to be made up of hemp because of its breathability and durability and also resistance to fungal growth and this hemp fibers are very lightweight, very durable. So they were more lasting for the farmers and as a result the fibers of this cannabis plant were used in making your jeans traditionally in America.

now because of the durability of this fibers they found application in your currency notes they found application in numerous other things like your filter pads and so on now while dealing with the drugs one disadvantage is cannabis the plants when they were cultivated or during the process of their harvesting they often yielded a resin a sticky residue which gave you a hallucinogen like activity From there on, cannabis also became a habit forming recreational drug.

So then what the cultivars did or what the government did is they kind of modified this plant. And during the process of modification, you would see that the habit forming activity of this plant is considered to be harmful. Due to a compound called as delta 9 tetrahydrocannabinol or often referred to as THC. So if you see the THC content on an average the THC content is between 0.2 to 0.3. So for a cultivar wherein the THC content well went below that because of genetic modification, the resin yield was decreased.

It was no longer habit farming and thus this type of cultivar was referred to as fiber type. Another cultivar which was kind of prized and kept only for its hallucinogen like activity and is often referred to as your drug type cultivar. In the drug type cultivar, you will see that the THC that is the concentration of delta 9 tetrahydrocannabinol goes from above 0.2 to 0.3% and generally considered to be above 0.3%.

Now this plant for its purpose that is for getting fibers as well as for getting drugs have been cultivated extensively in US. Not only in US it's been cultivated in Central America, Africa especially the East and South Africa and in Asia in countries such as India, Bangladesh, Pakistan as well as in Iran. Now, if you see this cannabis plant very particularly in terms of its drug like effects, the drug like effect comes from a resin and this resin is actually secreted from a tiny plant.

Hair like structures which are present referred to as trichomes. So cannabis bears two type of trichomes or two classes of trichomes. One which are called as covering trichomes. The covering trichomes are more hair like. The next one which actually secrete the resin.

are glandular trichomes. So the hair like trichome do one function and that function is to protect it from insects. So they form coverings on the stalks and on the leaves especially near the venations whereas if you see the flowering tops, the flowering tops are more secretory in nature and at those regions you will find glandular trichomes.

Now glandular trichomes in cannabis are also of two types so if you see the glandular trichomes you will see the ones with stock. Okay now this stock can be a multi-series that means lines of multiple cells forming multiple rows. So you have multiseries stalk and then they call it as a octacellular head. So somewhere you have your eight compartments done and this is your octacellular head.

So this one which is called as the capitate or headed stalk like a trichome gives you a majority of the resin and then little extent is given by what is called as your sessile glandular now sessile glandular is just the head there is no stalk that's the reason it is called as sessile glandular whereas the hair like structures are just kind of multicellular covering and that will prevent the insects from sitting on the plant

so you have this two that is the capitate one with the stalk and the sessile one this two type of trichomes are responsible for secreting resins the cannabis plant now based on this numerous numerous products of cannabis you find in your market now the one of the rich product or cannabis or resin rich product you find in market is ganja now ganja is Basically refers to the resinous tops.

Generally the flowering tops mostly the topmost portion twigs of unfertilized plants in preference the female plants are more preferred here. What is done is they are rolled. in ganja also you get two type of ganja to be more specific in the indian subcontinent the bombay ganja which is generally the pressed twigs so the twigs are collected and they are pressed

and the bengal ganja which is more of a twig which is rolled in the hands so you get two types of this ganja and this ganja are kind of sold for recreational purposes now when you take the other example the other example of your cannabis product is bhang the bhang generally you get during the festivities especially during the holy season what is done is both other twigs that is the new part of fresh part of the male as well as female plants is taken collected

and because it is a mixture of male and female plants you will see the female plants yield more resin. When you mix it with male plants the resin is diluted and doesn't have as strong an effect as your ganja. So bhang does have what is called as the recreational effect but it is much much lesser as compared to your ganja. So this bhang is often taken in or co-administered diluted in your buttermilk. So what happens in your buttermilk is you know that

Buttermilk is a lipophilic solution or what you call it as an emulsion to be more precise. So this bhang, the cannabinoids, whatever are there, when you triturate it with your buttermilk, the kind of compounds get dispersed in your buttermilk and when you consume them, they become more bioavailable. So in a way, we try to still get what maximum you can from the plant parts which are obtained. The next product which you get from cannabis in market is referred to as charas or hash or hashish.

Now there is some little difference but most of the words are used synonymously. Now what is done in case of charas is we know that the flowering tops of your cannabis contains your resin. So this workers pluck those flowering tops and often rub it in their hands. So as a result of rubbing what happens is whatever resin is being secreted is kind of stick or this resin sticks to your hand. Now this resin when you scrape it up it will contain exclusively your resin and very little of plant parts.

The only plant part which comes in the way is little pieces of your trichomes which get separated during the rubbing action and little pieces of stalk or very tiny leaflet that may be there. Now what is done is this is rubbed sometimes just to for the hygiene purpose and to get good yield instead of doing it with bare hands people take cloth, wrap your female

flowering tops in the cloth and then rub it. As a result because of its adsorbent effect the resin gets stuck to the cloth.

The flowery part is then removed and whatever is attached to the cloth is kind of scraped and then converted or filled into a square shape box. This square shape box is then kind of filled, pressed and then sold in market as your hashish cubes. Now if you go to the American side, you see a recreational drug often referred to as weed or marijuana.

This is nothing but same. It's your cannabis sativa. Now, what is done is the whole, you know, drug is taken very similar to your ganja. It's picked up. It's kind of mixed, dried and given as a mixture as a press now this can be then smoked or consumed as such but people generally prefer smoking weed or marijuana the reason is if you smoke the weed The bioavailability of your cannabinoids, the principle what we saw is your THC. The THC starts showing its action very immediately in about 15 to 30 minutes time. But whereas if you consume it orally,

By the time it goes into your digestive system, there on to your blood and there on to your CNS, it takes more than an hour. So people who want the immediate gratification, as you may say, or immediate high of consuming the weed, in that case, they prefer smoking the weed over consuming it. Now coming to a little safer options here the safer option is hemp like I said this is the genetically modified cannabis plant in which the resin content has been decreased to less than 0.2 and

as a result it has very low level of psychoactive substances and considered safe for consumption. Now that is safe for consumption. You can prepare products from that. One good product from that which comes out is hemp oil. Now, hemp oil is often referred to as cannabidiol.

The reason being, when the resin content is decreased. More focus has been given to THC. So as a result, the THC content becomes very low. And what is more active in hemp oil is CBD, often referred to as cannabidiol. So your hemp oil or the hemp extract, which is prepared from the extract,

By extracting cannabis with organic solvents and then evaporating it, that residue, often referred to as industrial hemp, is richer in CBD than THC. The hemp seed oil actually comes from the seed. So after flowering tops mature, you get a seed. The seeds are then pressed to get what is called hemp oil.

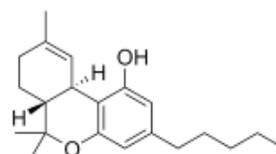
Hemp oil is a very good quality thin oil which you can use for other purposes. But it contains absolutely few or no cannabinoids. So it doesn't have that addictive property and doesn't give you CNS-stimulating or hallucinogenic effects. Now, coming to your chemical composition, what exactly is the chemical composition? The cannabis resinous compounds are obtained by condensation.

So you can see that your cannabinoids are making up almost 15 to 20% of the resin, and about 140 such cannabinoid compounds have been found in cannabis, principally THC and CBD. So if you carefully observe THC and CBD, what happens is if you cleave it here and then you start compensating this double bond here, you get a double bond right here, and this O is converted into OH. So nothing but your THC gets broken up and exposed to form what is called cannabidiol. But in the process, you will see that THC is much more potent compared to cannabidiol. So the net effects of the resin decrease when your THC content decreases. In addition to that, you also have what is called tetrahydrocannabinolic acid.

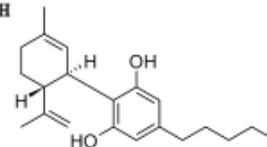
Chemical Composition

- Cannabis consist of 15 to 20% resin
- Over 140 cannabinoids have been found in Cannabis:
- delta-9-Tetrahydrocannabinol (THC), cannabidiol (CBD), tetrahydrocannabinolic acid (THCA), tetrahydrocannabivarin, cannabidolic acid, cannabinol (aged plants), trans-tetrahydrocannabinol etc
- volatile oil, trigonelline, and cholene.
- The main psychoactive cannabinoid in Cannabis is delta-9-THC.

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delta-9-Tetrahydrocannabinol (TH)



cannabidiol (CBD)

Then you have tetrahydrocannabivarin. Then you have cannabidiolic acid, and cannabidiol or cannabinol is also present. But it is present to a certain extent in aged plants or even after harvesting. If you keep it for more time, you can see more of this cannabinol appearing. Now, in addition to that, you also have your volatile oil, trigonelline, little amount of cholene.

The main psychoactive effect is definitely attributed to the presence of THC. Now, where do you apply this? Now, cannabis is applied for medicinal as well as recreational purposes. Now, cannabis, especially THC, works on cannabinoid receptors, specifically cannabinoid receptors 1 and 2. Now, if you see here, it predominantly acts on receptor 1, and that causes many of your CNS effects.

Whereas if you see cannabidiol, it acts on cannabinoid receptors 1 and 2 and has more other effects as well. And that's the reason cannabidiol or CBD is more preferred where you want fewer CNS effects but more of other effects, especially if a patient is in pain. You want, you know, pain-relieving effects. You want to reduce inflammation or decrease anxiety even without having those addictive or

high kind of effects or CNS stimulatory effects. In those cases, cannabidiol is more preferred. If you say THC, THC gives you more euphoria and hallucinogenic effects. Now, if you consume cannabis or marijuana as such, it is said that you cannot just pinpoint THC or CBD. The effects are more than obvious.

Your THC and CBD put together, the reason being there are more other compounds present, which are definitely your cannabinoid derivatives as well as other volatiles. Now, these total compounds give you what is called an entourage effect. So, a mixed reaction or what you refer to as a synergistic effect. Now, these synergistic effects can be felt not only on your CNS but also on your immune system.

Now, CBD is also being advocated. So, if you see, we said that you can genetically modify cannabis. Now, with genetically modified cannabis, your resin content is slightly decreased, especially your THC content. Now that the THC content is decreased and you have more of your CBD remaining, CBD, because it has a sedative, relaxing effect, is said to be therapeutically useful.

even traditionally your cannabis had some applications for treatment of CNS disorders so people are trying to prove that if you give it in a low dosage and balance your THC and CBD concentration, it can be a very good therapeutic compound for CNS disorders. In addition to that, cannabis can also be beneficial for people who are on cancer therapy, especially chemotherapy. Especially chemotherapy.

It is seen that with higher chemotherapeutic doses, the appetite is often suppressed, and people feel more nauseous. Now, because cannabis is a recreational drug, it is said that you can give cannabis to such patients. What will happen is that they now dissociate. With the pain, the pain is no longer as less to that chemotherapy.

They were found to have a better appetite. So, cannabis was proven to stimulate appetite and relieve nausea in such patients. So, in that way, you can advocate its beneficial effects. But definitely, it has more addictive effects, and that is the reason we have to weigh the pros and cons of this drug judiciously before making it legal.

Now we go on to the next resin drug and the next resin drug is a guaiacum resin. Now guaiacum is a very beautiful plant which is your guaiacum officinalis. And guaiacum is a resin which is obtained from the heartwood chiefly of Guaiacum officinalis as well as Guaiacum sanctum. Now, these are Zygophyllaceae family members, often found in the South American subcontinent and generally grown in tropical regions with very beautiful flowers, as you can see here in the image.

Now, if you are talking about Guaiacum officinalis or Guaiacum officinalis, it is more commonly found towards the coast of Venezuela, Colombia, and the western regions. Whereas, when you say Guaiacum sanctum, the Guaiacum sanctum is more native to Cuba, Haiti, the Bahamas, and Florida. Now, this Guaiacum resin is secreted throughout the world.

But if you compare it, The hardwood you know has almost you know yields up to 25% resin contains very little, just 2 to 3% resin, and as a result, it is more beneficial to extract the resin from the heartwood as compared to the softwood or sapwood. now this resin occurs as a very soft glassy brown rounded tears with very tiny two to three centimeter diameter

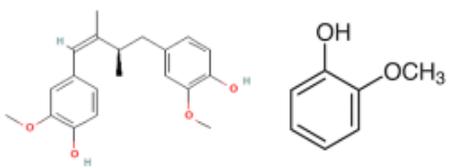
an acrid taste, and when warm, you will get a slightly aromatic taste. Now, how do you prepare this? Generally, what is done is the gum is naturally present in the wood. But if you injure the plant, you can get more of this resin secreted, and as a result, more resin will flow. So, generally, before cutting the trees, the plant is wounded by tapping to yield more resin. Now, because more resin is prepared, the plant is then cut so that the heartwood is rich with resins.

And in order to extract the resin from the heartwood, two things are done. Either the heartwood is heated. Now what happens on heating is the resin kind of melts and flows out. And this can be collected. Another option what is done is this wood chips are taken and boiled

especially in water containing salt and what happens is because of the density of salt water. this resin starts floating on it. So this floating resin is then sanded off and collected as your guaiacum resin. Now industrially one more method is used is they take the hardwood and extract it with solvents. Even solvent after extraction when you evaporate the solvent you get what is kind of called as cooled guaiacum resin.

Chemical composition

- Guaiacum resin mainly contains lignans.
- Guaiaretic acid, forms about 10% of guaiacum resin.
- guaiacolic acid, guaiacol and its derivatives),
- volatile oils - guaiol and cadinene
- Guaiacum is soluble in alcohol, chloroform and solutions of alkalis.
- An alcoholic solution gives a deep blue colour (guaiac-blue) on the addition of oxidizing agents such as ferric chloride



Guaiaretic acid

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Now this guaiacum resin contains numerous lignan derivatives. So far what we have seen is

your resin contains oxidized terpene derivatives but here you will see it also contains in addition to your terpene derivatives lignans. So you have what is called as guaiacolic acid which makes up almost 10% of the guaiacum resin. If you cut it here you get what is called as your guaiacol.

So you have your guaiacetic acid, you have your glycol and this glycol polymerized with other compounds and forms glycol derivatives. You have your gualol and cadenine which are slightly volatile. Now, if you see your guaiacum resin, it also contains another derivative, which is important and used for diagnostic purpose. And that is your guaiacolic acid, especially the alpha guaiacolic acid, which gives you a numerous reactions with blood.

And it gets oxidized to form a blue-colored compound. Now, this guaiacum resin is soluble in alcohol. It's soluble in chloroform and also in alkalis. When I say your guaiacolic acid, this guaiacolic acid gives you a deep blue coloration often referred to as your guaiac blue when it is oxidized.

So whenever you add metals such as ferric chloride, your, especially alpha guaiacolic acid, turns into a blue-colored derivative. Now, this is something that can be used for the detection of oxidizing compounds. So where do you apply this? So this oxidation, as you can see, your guaiacolic acid will undergo oxidation with the heme.

So you know there are cases or disease conditions in which your intestine bleeds. And whenever you have intestinal bleeding, this blood often accumulates in your stool. So you have what is called a fecal occult blood test. So you have to check whether blood is also coming out in your fecal matter. In that case, what is done is a filter paper test wherein a paper is dipped in your stool.

guaiacum resin or guaiacolic acid is used so especially a guaiacum coated filter paper is used is treated with the stool samples, and you allow it to see the reaction. We know that guaiacolic acid gives you a bluish-colored complex, especially with metals such as iron. So you know, in your blood, especially in your hemoglobin, you have iron in the heme region. So if there is blood present in the stools, this iron will react with alpha-guaiacolic acid to give you a blue color complex, and this filter paper will detect the blood in your stools. In addition to that, your guaiacum resin is registered as a food additive. With E number E241,

especially for its preservative effects, and E number E314 for its antioxidant effects. Traditionally, guaiacum resin is used or still used in the case or treatment of syphilis. But apart from that, it is used in conditions such as gout and rheumatism.

It is also used in the treatment of arthritis, asthma, tuberculosis, and malaria. So here are a few more references if you wish to know more about this compound, such as cannabis and guaiacum. And thank you for your patient listening.