PHARMACOGNOSY AND PHYTOCHEMISTRY

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Week 10

Lecture46

Week 10: Lecture 46: Introduction to Quality Control of Herbal Drugs

Thank you. Hello, dear learners, and welcome to week 10 of the NPTEL course in pharmacognosy and phytochemistry. We started our course with the definition of pharmacognosy and phytochemistry. Thereafter, we learned different classes of phytoconstituents every week. Now, in this week as well as in the forthcoming weeks, we will try to understand the methods for quality control of herbal materials.

So before we proceed, what we studied in the previous sessions were different examples of drugs containing various sets of secondary metabolites, often referred to as phytoconstituents. Now, depending upon these phytoconstituents, they have different applications. Now, depending upon the applications, the herbal drug industry starts converting these plants into medicinal products. Some of them call them herbs. Some of them call them herbal medicines.

Some of them are called herbal medicinal products. Many of these terms are used synonymously as well as among the common people in the herbal drug industry. So when I have to communicate with you, I say, let me give you that herbal drug sample or let me give you that herbal medicine. So what exactly do I mean?

Let's first try to understand these terminologies, and then we will go into the quality control methods. So when I refer to or when I call it herbal substance, herbal substance is any product which is made up of plant parts. So when I say vasaka leaf, that means it's a plant part. That is, it's the leaf of adhatoda vasaka. When I say it is acacia, it is a gum.

That means it is a gum which is obtained by making an incision from the acacia plant. So herbal substances are actually products which are obtained from plants, including both organized and unorganized drugs. The organized drugs include plant parts such as fruits, stems, leaves, and other parts not mentioned here, like flowers, pollen, or in some cases even fruits and seeds. As well as unorganized drugs, chiefly untreated exudates, such as gums, mucilages, resins, etc. A few examples of such herbal substances are vasaka leaf, acacia gum, opium latex, and so on.

The next terminology is herbal preparation. Now, this is when you take your herbal substance and process it further by applying numerous processes. These processes can be as simple as extraction, like when you prepare your tea. You take your tea powder and boil it. That's called your tea extract.

So you can do an extraction. You can do a distillation. You can do a fractionation. You could run column chromatography and do a purification, or you can take the drug and do something called fermentation. Now, all this processing

takes your herbs or herbal substances a step forward into making them a good product. Such preparations or products are often referred to as herbal preparations. So herbal substances are natural substances that you obtain directly from nature, whereas herbal preparations are those where mankind is involved in processing them. Either extracting, distilling, or converting into something—say, for example, your jatamansi oil: you take jatamansi root and distill the oil, or papaya leaf extract: you take the papaya leaf, juice it, and thereafter dry it. That is, there is a human element involved, and such ingredients in the market are referred to as herbal preparations. Now we go to the next definition. The next definition is herbal medicine or herbal medicinal products. These are products that you actually see on the counter, looking like your allopathic medicine.

Now, take for example here I have your Senna tablets. Senna, as we studied, contains anthraquinone glycosides, which are used as laxatives. Now, convert them into tablets by using binding agents and disintegrants. That is, I take a drug, add excipients, and formulate it in a way that is very consumer-friendly and can be used directly. In that case, I refer to my product as a herbal medicinal product.

So those are finished, well-labeled, over-the-counter products, which may include simple substances, that is, your herbal substances. So even though you can have your shatavari powder, imagine it in a container that is ready for consumer use, so I can consume my shatavari powder directly from it. It is well-labeled. How should it be stored? How should it be kept?

Such cases or such products are referred to as herbal medicine. So it includes all your aerial plants as well as underground parts. You can take the drug or drug combinations, like your triphala churna, which is a combination of three fruits. You can have them in a crude state, like your acacia powder, which is to be taken, or isabgol powder, or you can have a preparation that is made, like we saw with the oils or blends. Now, this also includes a lot of unorganized drug material, which includes your juices, gums, fatty oils, essential oils, and other substances.

They often contain excipients to make them consumer-friendly and are in a state that is ready to administer. Good examples of this include your Triphala Churna, Ashwagandha powder, or your Senna tablets as well. Now, with this, we move on to our next important term, and that is the botanical reference standard. Now, we say that whenever you purchase a drug from the market, You have to know what it is.

Say, for example, if I go to purchase a new vegetable from the market, I should have a predetermined notion of what exactly I am buying. Otherwise, I may purchase something else. So, the herbal drug industry is very huge. There are numerous herbal drug substances which are official in different forms of traditional medicine. So, we have our Ayurvedic, we have our Siddha, we have our Yunani, we have our folklore medicine, and in such cases, if you just put them together, there are thousands of herbs.

And in some cases, it's humanly not possible to know thousands of herbs just by visually looking at them. In that case, there are substances which the industry keeps for record, so that tomorrow if I have to purchase this, it should look like this. Such substances are called botanical reference standards. So, imagine you are going to purchase an orange. Before that, your parents show you, you know, this orange in the market should look something like this.

Specifically or exactly, that is what the herbal industry does. They give us what are called botanical reference standards. These are reference standards of the most ideal drug, what your sample should look like. So, these botanical samples or botanical reference standards help us ensure identity. They help us ensure purity as well as the composition, which are very vital for quality.

Now, whenever an industry keeps a botanical reference standard, that is a standard which is well characterized. That means if I show you an orange before I tell you to get an orange from the market, I myself will make sure that this is the genuine orange. How do I do that? I do some evaluation which includes physical, chemical, maybe DNA, and genetic aspects. I'll see some molecular characteristics, and everything is validated.

So you can see a botanical reference standard in the image here. That's Calendula officinalis, which is used as an anti-inflammatory drug, often found in many of your anti-inflammatory balms or lotions. Here in this case, it is DNA barcoded. What does that mean? That means even the genetic makeup of that botanical reference standard has been tested for identity.

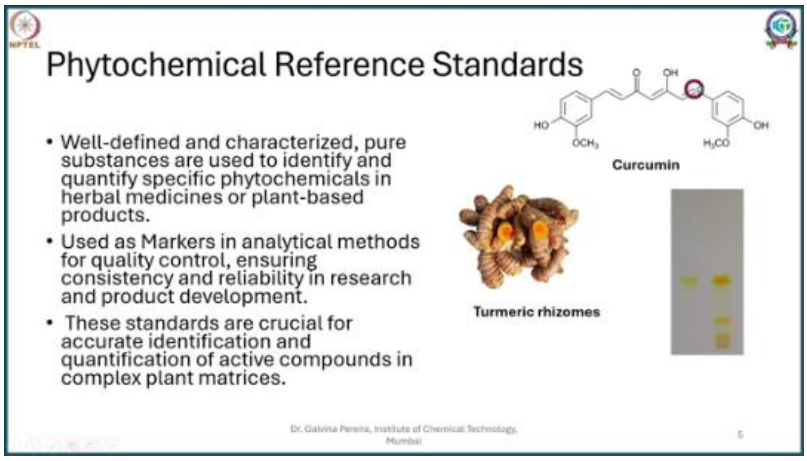
So only when the DNA matches, I can tell you that this is the orange I want. So this is the calendula that the industry wants for its use in herbal preparation. So botanical reference standards are associated with different parameters, which will help us assure the quality. So once you get an orange from the market, I will compare it. And I will come to know how genuine it is.

And that's what your botanical reference standards are for. Similar to that, we have another set of standards which are called phytochemical reference standards. So far, in every chapter, we've been studying different classes of phytochemicals. Now, these phytochemicals may be your alkaloids, glycosides, tannins, and so on. Now, what happens is every drug contains some of them in a unique way, some of them in a similar way.

Now, say for example, when I mention gallic acid, there will be many drugs containing gallic acid. But if I say, you know, meconic acid or tropane alkaloids, there will be few plants which contain tropane alkaloids. So they are what are called markers. So these

marker compounds are often used for analysis. Now here, what we have is a very simple example, and that's your turmeric.

So in your turmeric, you have your pigments, which are your yellow pigments, and these yellow pigments are curcuminoids. Okay, so curcuminoids are a mixture of three pigments we saw, and the chief one among them is your curcumin, the structure of which is drawn here. Okay. So this is curcumin, and if you recollect, when you remove this methoxy, you get dimethoxy curcumin. When you remove both of these methoxy groups, you get what is called bis-dimethoxy curcumin. So this mixture of three pigments is very much characteristic of Curcuma longa or turmeric plants.



Now, if I have to standardize that, what will be my reference standard for these pigments? Curcumin is the major one. So, of these three pigments in terms of composition, as you can see here, even in the TLC, your curcumin. You have your dimethoxycurcumin and then you have your bisdimethoxycurcumin, of which the major one is curcumin. So, this I will use as my reference standard.

But in order to get that as a reference standard, I have to have something to compare it with. And those compounds are called phytochemical reference standards. So industries often will purchase, procure, or purify and keep this curcumin. And this curcumin will serve as a standard. So every time they get a new turmeric sample, they are going to run a TLC.

They are going to spot curcumin here and they are going to run the turmeric extract here. So what you get in the process is you will be able to see if it is genuine turmeric or not. So they help us not only to check the genuineness, that is the identity. They also help us to quantify. So if we subject it to analytical methods such as your colorimetric estimation, say for example, I have my standard curcumin and 10 micrograms of curcumin gives me an absorbance of 0.5.

Now, if I check my turmeric extract again, I will get the same kind of absorbance values. Say, for example, 0.5, then I will say that my turmeric extract also contains 10 micrograms per ml. So, I can also know the concentration. I can quantify it by UV, I can quantify it by TLC, specifically HPTLC, I can quantify it by HPLC, UPLC, and so on. So, not only do these phytochemical reference standards help in identification, they also help in quantification. So, tomorrow, I have a bad sample.

Normally, if you see, the curcumin content ranges between 2 to 7 percent. So, if I have a bad sample which has just 1% curcumin, I can reject the drug. Or, if I have a really good sample which has a curcumin content of 7%, I know that is the one I have to purchase because it's a good-quality one. So, they help you in maintaining product consistency as well. One batch has 7%, another batch of turmeric rhizome has 2%, and another batch has 3%.

So, that will lead to a huge variation in my product. So, these determinations or these phytochemical reference standards help me in analysis and thereafter help me maintain the consistency of my product. Now, we move on to quality control. What exactly is quality control? Quality control is a method which I will do or carry out to check whatever is given to me.

Does it match the description of that? So if you tell me you want to get a tulsi leaf, So is it really a tulsi leaf that you're giving to me? What can I do to check if it is a genuine tulsi leaf? I will call all those things quality control methods.

So we have the World Health Organization, and the World Health Organization defines the term quality control as the sum of all procedures, whatever you can do, the sum of all procedures that are undertaken to ensure that the identity and purity of a particular

pharmaceutical are there. So, for example, let's just refer to our tulsi. So, identity: is it the genuine tulsi I am looking for? And purity: So, if I have 1 kg,

Is it all 1 kg of tulsi leaves, or is it 800 grams of tulsi leaves and 200 grams of something else? So, quality control includes all the methods that we will carry out to ensure the identity, purity, and when we say purity, we also refer to content. Now, why is that important? These three components, once ensured at the entry level itself, will help us gain a quality product. Now, entry level means right from the farming stage.

So you have to maintain good quality of your plant to get a good quality product. And then once all of this is ascertained in terms of my raw material being good, then my product is definitely going to be good. So quality control methods are methods to ensure your identity, content, as well as purity of the drug substance. Now, why is there a need for quality control? The need for quality control is basically based on three principles.

The very first principle is consistency. See, when I am doing an allopathic preparation such as aspirin or paracetamol, when I am preparing a 500 mg tablet, I know that tablet is bound to contain 500 mg of paracetamol, excipients apart. Now what happens in plants is, if I am not able to match up, I cannot say that my amla every time is going to contain 1% gallic acid. The consistency of my product changes. So quality control will ensure that the consistency of my product remains.

Whatever I consume should be safe. Safe, because if I consume something which is unsafe, that is going to be detrimental to the health of my patient. And next, efficacious. Now, most of the preparations or herbal preparations people just take because they are safe. Very rarely people say that I take this herb because it is more efficacious as compared to allopathic. We hardly find such definitions. I put the efficacy last, but it's not the last. That's a very important part. Your drug should be efficacious. When you ensure consistency, when you ensure safety, when you ensure the content of your phytochemical is good, it will show you the therapeutic effect. That means it is going to be efficacious.

This efficacy is seen by testing it on animal models, humans, as well as on cell cultures. Now, let's delve a little deeper into these quality control parameters. So, what is

consistency? For consistency, I have to ensure that whatever raw material I am receiving in my industry is authentic. When I say authentic, that means it should be genuine.

What I asked for is an orange, and what I get is an orange. OK, so now authenticity is very vital because that will give me the remaining two. That is your safety and efficacy. Now, when the drugs are not authentic, that may be due to adulteration.

What is adulteration? Adulteration is when you intentionally or unintentionally add something more. Say, for example, you add brick powder to your chili powder—that is a classic case of adulteration. Or maybe you must have come across, for your turmeric itself, people add dyes such as methanol yellow so that the haldi looks more intensely yellow in color. That is what is called adulteration. Substitution is when I replace it—I substitute for it. OK, so imagine I have chandan ka wood, but instead of chandan ka wood, I am selling something else. That is, I am selling plain cedar wood or some other cheap-quality wood.

I substitute it and that is very bad. The last case is spurious wood. Spurious is you might have come across many spurious products in market. Spurious is I'm giving you something. I'll say that, you know, probably this is a product which Himalaya has made and this is very good.

And actually, it so happens that either this company which has prepared doesn't exist. Either the product is misleading. I tell it's an ashwagandha powder, but actually it is something else. And what happens is this all are labeled as your spurious. So when I'm doing quality control, I have to ensure that I have to have an authentic drug, which is free of any adulteration, substitution, which should not be spurious in terms of product.

Now consistency can also vary due to content variation. Now this is something which is unintentional. Like I said say for example when I am talking about amla I require 1% of gallic acid in it. Now in some cases I might get a batch of raw material of amla powder which might not have 1% of gallic acid. Now, the reasons for that could be basically categorized into two parts, intrinsic factors and extrinsic factors.

Now, intrinsic factors are more to do with the plants. Imagine you have a huge farm of amla, but due to certain disease, certain infestation, some mutations happen, or you know,

your farm has been there for ages and now it is all grown old. The plants are no longer as vigorous as they were previously. The content of your actives goes low, and that's where, in pharmacognosy, when we were saying acacia, we said that it's better to tap it between six to eight years of age. Beyond 8 years, the gum is not as good. Or when you are even taking out gum, just see that the first few tappings are good. Later on, the quality of the tapping becomes weak. What happens is, due to age, disease conditions, mutation, and a lot of other factors, the plant itself will secrete less amount of gallic acid.

That is also leading to your content variation, and that will change the consistency of my product. Similarly, sometimes the factors are not in the plant, but they are in the external environment. This includes climate. Imagine too much rainfall or too little rainfall; the soil changes. You know, sometimes it is conducive, sometimes it doesn't have any humus, minerals, or any support nutrients.

And as a result, the yield of your metabolites will fall less. Presence of other crops, which kind of eat up the nutrition, and then they'll harm it. And if you're not replenishing the ground, you're kind of using the same field over the period of years. Suddenly, what has happened is all the nutrients of that particular plot have gone in. And that will lead to a decrease in yield.

So the consistency of the product will vary, and there are a few factors for which it will vary. Another reason, or another way to see quality control, is to ensure safety—and when I say safety, I mean I have to be safe or I have to keep my product safe. Now, this product sometimes intentionally or unintentionally contains hazardous substances. Now, these hazardous substances can include pesticides, We are very cautious about having or detecting pesticides in our food and drinks.

But imagine that can happen in your medicine as well, if your medicine is a herbal product. Just to protect it from infestation, the farmer might have sprayed pesticides. And what happens is, during the course of processing, these pesticides will get concentrated and end up in your medicinal product. Similarly, if you have plots or farms in places where radioactive substances have been mined or radioactivity has been used, there is a good

chance that these substances will also carry some residual radioactivity. That is not at all desirable and is harmful to our health.

Previously, we also saw aflatoxins as fungal metabolites from aspergillus. They cause food poisoning, and you may recall liver cirrhosis and cancer. So a fungal infestation that could lead to the deposition of aflatoxins is something we don't want in our product to ensure safety. Similarly, we don't want any pathogenic contamination. See, we don't consume our products or drugs in the most sterile form.

We don't sterilize our food before consuming it, right? Similarly, our drugs need not be sterile if you are taking them orally. But it is necessary to ensure that the microbial load is minimal. It is necessary to ensure that there are absolutely no pathogenic microorganisms that can cause disease. So we also check or ensure that microbial contamination is minimal and that pathogenic organisms are absent.

Apart from that, it should be free from foreign organic matter. This includes other plant parts, animal excreta, and similar contaminants. There should be no cockroaches in your products. We don't want any animal products, such as flies that may have infested the drug, leaving behind wings or other residues. These are all treated as foreign organic matter. Their metabolites or byproducts may pose a health hazard.

To ensure safety, we must verify that hazardous substances such as pesticides, radioactive contamination, aflatoxins, microbial contamination, or foreign organic or inorganic matter like soil are absent from our product. For efficacy, we know that only potent substances will work, which is why efficacy studies are necessary. Quality control is guided by certain reference books and standards. Quality control is regulated in different countries by various guidelines. The most commonly followed standards are pharmacopoeias. Every country drafts its own official pharmacopoeia.

So for India, we have our Indian Pharmacopoeia. For America, they have the US Pharmacopoeia. For Europe or for England, they have the British Pharmacopoeia and so on. So every country will have its own pharmacopoeia. They will lay down the guidelines.

If Vasaka is to be there, these have to be the quality parameters for Vasaka. Similarly, taking into consideration the developing countries, WHO also came forward and laid down guidelines, which are a kind of minimum benchmark. That means your compounds or your drug substances should at least adhere to these guidelines. And then that is included in the WHO monographs of these herbal substances as well as WHO quality control methods. Now, the Indian Council of Medical Research has also come out with its own version of herbal monographs to ensure safety.

And they also contain detailed quality control procedures. So with this, in the next session, we'll go deeper into methodologies. But here are a few references if you wish to know why we should do quality control. And thank you, everyone, for your patient listening. Thank you.