2.3.2: Teachers use ICT enabled tools for effective teaching-learning process

SUMMARY OF DOCUMENTS

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CHAPTER 4:
NATURAL PRODUCTS USED AS PHARMACEUTICAL EXCIPIENTS AND OF ALLIED INDUSTRIAL UTILITY

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A] Natural Colors and Dyes

Color

→ To denote the human eye's perception of colored materials

→ **Color may provide an indication of chemical changes in a food, such as browning and caramelization.**

Pigment

→ Normal constituents of cells or tissues (**which is synthesized and accumulated in, or excreted from, living cells)** that impart color.

- **Colorant**

→**A general term referring to any chemical compound (synthetically made) that impart (communicate) color i.e. dye and lake.**

- **Dye**

→**Colorants used in textile industry, has no place in food usage.**

- **Lake**

→**A food colorant is synthetically made and added to processed foods**

→**referred to as certified colors**

Mordent

- As early as the Egyptians, it was known that other substances caused some dyes to bind that normally would not. These are called mordents.
- Sometimes mordents came from the container in which the dyeing was being done .
- Alum is a commonly used mordant.

Mordents

Mordents are chemicals which help the dye molecules bind to the fibers. Iron, copper, chrome, alum, and urea are often used with plant-base dyes.

CHEMICAL CLASSIFICATION

- **1. Basic or Cationic Dyes**

✓ This group was the first of the synthetic dyes to be taken out of coal-tar derivatives.

✓ The name means that these are dyes with an organic material, which is soluble in a simple acid.

✓ Basic dyes were originally used to color wool, silk, linen, hemp, etc., without the use of a mordant, or using agent.

✓ Nowadays basic dyes are no longer used to any great extent on cotton or linen and seldom on wool.

- **2. The Direct Dyes**

✓Direct dyes can be used on cotton, linen, rayon, wool, silk and nylon. These dyes usually have azo linkage –N=N- and high molecular weight.

✓They are water soluble.

- **3. The Acid Dyes**

✓This is a very large and important group of dyestuffs.

✓While an acid dye is a salt the color comes from the acidic component, while in the basic dye it's from the organic base.

✓The first acid dyes were combinations of basic dyes with sulphuric or nitric acid.

- **4. The Sulphur Dyes**

✓The sulphur dyes provide very deep shades, which have excellent resistance to washing but poor resistance to sunlight.

✓Sulphur dyed fabrics usually must be treated with alkalis to neutralize the acids, which have formed.

- **5. Azoic Dyes**

✓These dyes are used primarily for bright red shades in dyeing and printing

✓Azoic dyes, called Naphthols in the industry, are actually manufactured in the fabric by applying one half of the dye.

- **6. The Vat Dyes**

✓The term vat comes from the old indigo method dyeing in a vat: indigo had to be reduced to light form. Vat dyes are made from indigo, anthraquinone and carbazole.

✓**Soluble Vats:** There are no water-soluble preparations for dyes.

✓**Indigo:** The oldest known vat dyestuff, formerly made from the indigo plant, but now made synthetically.

- **7. Collective Dyes**

✓Collectives are the latest dyestuff and because they react chemically with cotton, viscose, linen, wool and silk they are very fast to washing treatments.

- **8. Dyes for Manmade Fibers**

✓Each new fiber, as it emerges from the laboratory, must be carefully analyzed and tested for its reaction to different dyestuffs.

✓**Alizarin Dyes:** These are vegetables dyes, originally derived from the madder plant and now produced synthetically. They produce a brilliant turkey red, among other colors.

✓**Aniline Black:** They are produced from the chemical aniline, and are usually associated with the color black.

✓**Chrome Dyes:** These are a special type of acid dyes and they are used to color animal fibers, especially woolens.

- **9. Neutral Dyes:** These are metal containing acid dyes and the metal is added in manufacture.
- **10. Types of Natural Dyes**

Natural dyes can be sorted into three categories: natural dyes obtained from plants (Indigo), those obtained from animals (cochineal), and those obtained from minerals (ocher).

- **1) Natural dyes obtained from animals**
- A good example is cochineal, which is a brilliant red dye produced from insects living on cactus plants. In fact, most cherries today are given their bright red appearance through the artificial color "carmine ", which comes from the cochineal insect.

- **2. Name of Dyes from plants- Major Natural:**

ANNATO is from the pulpy part of the seeds of Indian plant. Bixa orellana : Fugitive orange red color.

BRAZILWOOD is from wood of the tree, Caesalpinia Echinacea: bright red color.

CUTCH is obtained from boiling the wood of Acacia catechu, native to India: rich brown color.

INDIGO is obtained from the plant, Indigofera tinctoria: blue color.

KERMES is extracted from bodies of tiny insect, Coccus arborum ; red dye.

LAC is obtained by boiling tree incrustation produced by tiny lac insect. Tachardia lacca ; bright red color.

MADDER comes from the roots of the plant, Rubos tinctorum ; red color. Produces alizarin.

- **3. Names of Dyes from plants, minor natural :**
- BABUL TREE, *Acacia scorpioides.*
- BAEL TREE, Aegle mermelos.
- INDIAN MADDER, Rubia cordifolia.
- HENNA PLANT, Lawsonia inermis.
- POMEGRANATEA. Punica granatum.
- RED SANDLEWOOD, Pterocarpus santalinus.
- TAMARIND TREE, Tamarindus indica.
- TULIP TREE, Thespesia populnec.

- **Properties of Dyes**

✓The properties of dyes are based on the following factors:

✓Shade (brightness or dullness)

✓Fastness Requirements

✓Level Dyeing Properties

✓Ease of Application

✓Dusting

✓Environmental Concerns

✓Ease of application, durability of color, and resistance to sunlight and chemicals are important properties that are considered when selecting a dye for use.

- A good dye has the following qualities:

✓It has a suitable color.

✓It fixes itself to fabrics.

✓It has fastness properties

1. COCHINEAL

- Source
  - Extracted from cochineal (*Dactylopius coccus costa)*

Cochineal Extract

- Stability
  - Light: excellent
  - Heat: excellent
  - pH: poor
    - Orange in acidic pH
    - Purple in neutral pH
    - Blue in alkaline pH

- Acid stable cochineal extract:
  - Can be boiled in 10% citric acid or even 0.01N HCl for at least 3 hrs.
  - Dose not precipitate in acidic beverage → precipate cause discoloration.

Cochineal Extract

Left: Control (An acid proof cochineal extract) in 0.3% citric acid solution.

The original red color faded away after exposure.

Center: ACRC 1162-ralb in 1.0% citric acid solution. The original red color did not fade.

Right: ACRC 1162-ralb in 0.01N HCL. The original red color did not fade.

2. Henna (*Lawsonia inermis*, Lythraceae)

- By 3000 B.C., Greek women used henna (Lawsonia inermis, Lythraceae) to dye their hair. The leaves are ground into a paste that has a great affinity for protein.
- Henna is still used in hair preparations.

Dyeing the skin with henna is practiced in many Near Eastern countries.

3. Achiote or annatto,
(*Bixa orellana*,
Bixaceae)

Achiote or annatto

Achiote or annatto, *Bixa orellana*, Bixaceae

- Achiote or annatto, *Bixa orellana*, Bixaceae, was used by the Aztecs and Mayans for food preparation.
- The plant is probably native to Brazil.
- The pulp surrounding the seeds contains a lipid dye that is soluble in grease and dyes foods a yellow-orange-red color.

- Achiote is widely used in Latin America, but also in other parts of the world today.
- This substance is also now used to dye margarine and similar products.
- Achiote contains about 2% vitamin A.

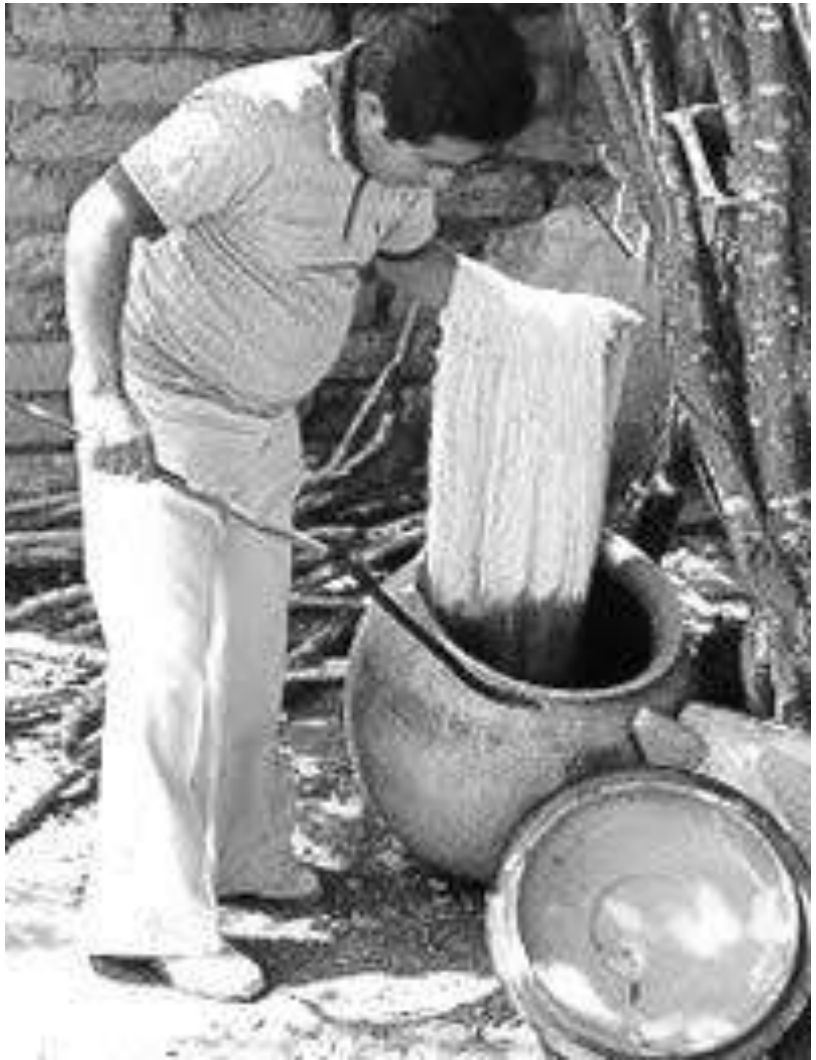
4) Indigo (*Indigofera tinctoria*, Fabaceae)

- The sludge of partially rotted plant material which settles to the bottom is collected and pressed into cakes.
- When dry, these cakes produce a powder that makes a colorless solution.
- The color only develops when an item is dipped into the solution, removed and then exposed to air.

Submerging indigo foliage under water to manufacture indigo

Indigo dye ready to be added to the dye bath

When the fabric is first removed from the bath of indigo dye, it is not blue, but turns blue upon oxidation by air.



- Indigo was an early crop in colonial South Carolina. South Carolina indigo was considered excellent, but as the economics were not too good, it was replaced by rice.

- The leaves contain about 3% indigo.

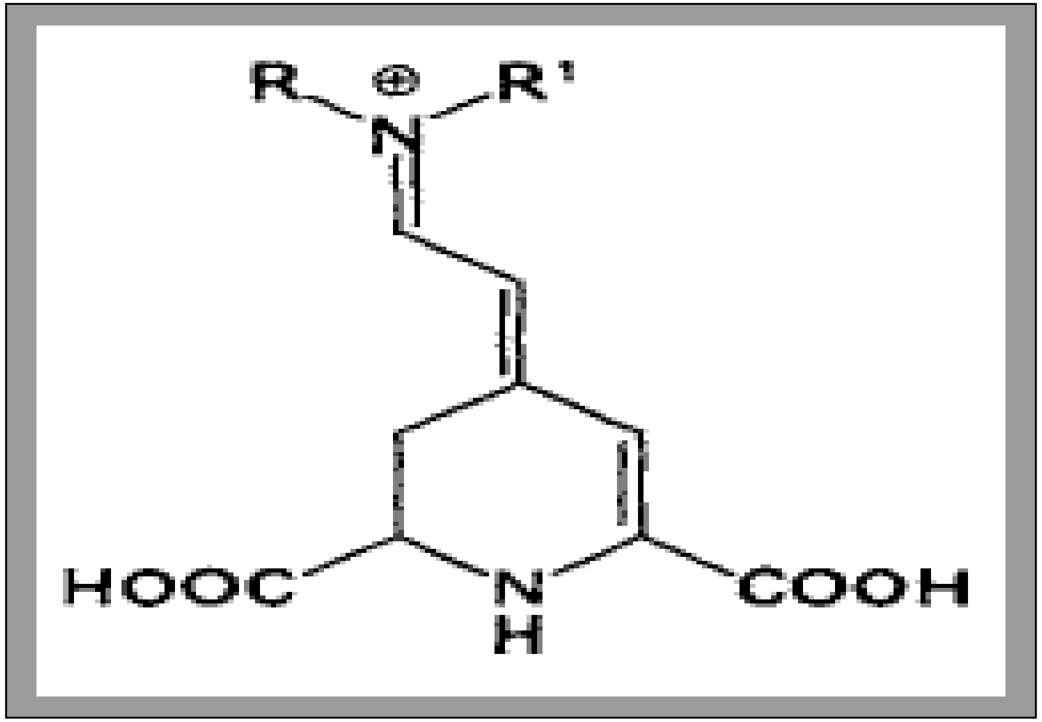
- Synthetic indigo was produced in 1897.

5. Beet

- Plants containing betalaines have colors similar to plants containing anthocyanins.
- The presence of betalaines in plants is mutually exclusive of the occurrence of anthocyanins.
- They consist of **red-violet** betacyanins and yellow betaxanthins.
- Their color is not affected by pH, contrary to the behavior of anthocyanins.

- Betalains are water soluble and exist as internal salts (zwitterions) in the vacuoles of plant cells.

- The general structure of betalains:



- About 50 betalains have been identified. The majority have an acylated sugar moiety.
- The acids involved are sulfuric, malonic, caffeic, sinapic, citric and *p*-coumaric acids.
- All betacyanins are derived from two aglycones:

  betanidin and isobetanidin.

Betanin

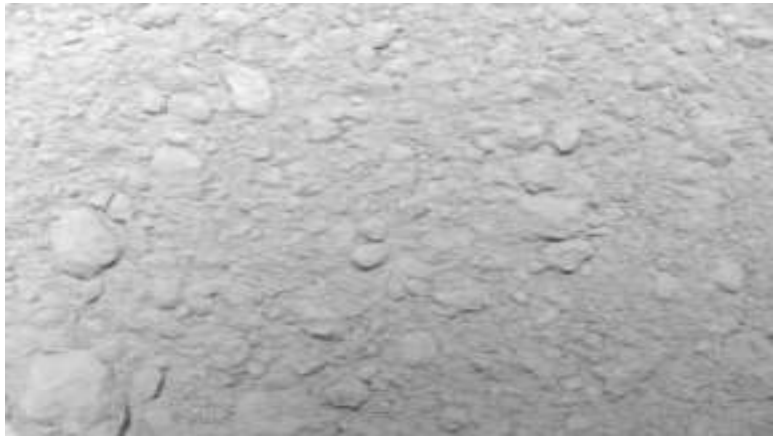
- Betanin is the main pigment of red beet. It is a betanidin 5-0-β-glucoside.

- ## 6) TURMERIC

- Turmeric (*Curcurma longa*, Zingiberaceae) is used mostly today to color foods (such as pickles), but has been used to dye clothing.

Turmeric Oleoresin (Curcumin)

- Source:
  - Extracted from *curcuma longa* L., a member of ginger family.



- Coloring component:
  - Curcumin and curcuminoids
- Solubility
  - Fat and alcohol soluble
  - Cold water insoluble
  - Commercially dissolve curcumin in polysorbate-80 or –60 to make it water dispersible

Turmeric Oleoresin (Curcumin)

- Stability:
  - Heat: good
  - Light: poor
  - pH: color hue change with pH
    - Greenish in acidic pH
    - Orange yellow in neutral pH
    - More stable in acidic pH than in neutral or alkaline pH

- Color: Bright yellow in acidic solution

Turmeric Oleoresin (Curcumin)

- Applications:
  - Pickle
  - Bakery
  - Confectionery
  - Others

- Snack
- Pudding
- Gelatin
- Yogurt
- Popcorn
- Finger foods

B] NATURAL SWEETENERS:

Natural sweeteners are Real Food, meaning they’re old and they’re traditional.

As such, our bodies are better equipped to eat them.

Usually, natural sweeteners don’t cause as large a change in insulin levels as artificial sweeteners, so they’re less likely to contribute to insulin resistance and over burden your pancreas.

On a practical level, that means they can reduce your risk for developing diabetes.

- **Nutritive and Non-nutritive Sweeteners**
- Sweeteners are divided into two groups:

those which have calories and provide nourishment (nutritive) and those that are calorie-free (non-nutritive).

- Nutritive sweeteners such as sugars and sugar alcohols add carbohydrates to food and calories to your diet that contain few vitamins or minerals - hence why whey are often referred to as 'empty' calorie foods - whereas non-nutritive sweeteners do not.
- This is the main difference between the two and is important to remember when comparing the contents of foods and beverages.

- **Nutritive Sweeteners - Sugars**
- When eaten in moderation with a mixed meal and as part of a healthy overall diet, sugars are considered fine and do not cause special problems for people with carbohydrate intolerance such as diabetes mellitus or insulin resistance.
- **Types of sugars**
- **Sucrose** ; **Fructose** ; **Dextrose**; **Corn Sugar** - Also known as corn syrup, **High Fructose Corn Syrup** - Sweeter than sucrose; **Maltose**; **Honey**
- **Sugar Alcohols**
- Sugar alcohols are a type of carbohydrate called "polyols" which are used as alternative food sweeteners to natural sugars.
- **Types of Sugar Alcohols**
- **Sorbitol**; **Xylitol**; **Mannitol**; **Hydrogenated Starch Hydrolysates (HSH)** - Derived from corn, wheat or potato starches

- **Non-nutritive Sweeteners**
- Non-nutritive sweeteners, or artificial sweeteners as they are also commonly referred to, are a key ingredient of dieting products as they provide a significant sweetening effect without adding carbohydrates or calories.
- Due to their strong sweetening effect - artificial sweeteners are many times sweeter than sucrose (table sugar) , although high intakes of some have been linked to increased cancer risk in the past
- **Types of Non-nutritive Sweeteners**
- **Saccharin**
- previous animal-based studies on saccharin linked high intake of the sweetener to increased risk of bladder cancer.
- **Aspartame**
- is 200 times sweeter than sucrose. it is not stable in heat or for long periods in liquid form, and is therefore not used in cooking.
- **Sucralose**
- Derived from sugar. Research shows it has no effect on blood sugar and is deemed safe for use in all age populations.
- **Cyclamate**

Taste Modifiers

- Taste Modifiers are in particular those which produce a sweet taste from none sweet foods (by tracking the mind).

The 3 main Taste Modifying plants which are well known are:

1. **Miracle Fruit or Miracle Berry (Synsepalum dulcificum)**

- ✓ **The active ingredients in Miracle Fruit is the protein named Miraculin. It makes sour and bitter foods taste sweet.**
- ✓ **The Miracle Berry is also being grown in the USA as well as Taiwan.**
- ✓ **Currently Miracle Fruit is being sold as Miracle Berry Tablets and can be purchased from Taste Trips**

2. Curculigo Latifolia

- ✓ **Curculigo Latifolia (Lumbah) is a fruit which grows natively in Malaysia.**
- ✓ **It has the same property as the Miracle Fruit, only Curculin the active ingredients in this fruit, also makes WATER taste sweet.**
- ✓ **Curculin is a Protein and is therefore destroy at high temperatures just like Miraculin.**
- ✓ **Curculin is also SWEET itself, unlike Miraculin which is not sweet by itself.**
- ✓ **Curculigo has to be freeze dried right after picking for the magical property to stay intact.**

3. Staurogyne Merguensis

- ✓ **Staurogyne Merguensis is different than the other 2 plants, in that, the taste modifying protein is in the leaves and also that the taste modifying substance is not a protein. A Glycoside known as Strogin is the active ingredients in this plant. The strogin makes water taste sweet.**
- ✓ **The advantage of Strogin is that, if the leaves are dried they can be preserved at normal temperatures.**
- ✓ **unfortunately this plant is very rare.**

1. Serendipity Berry

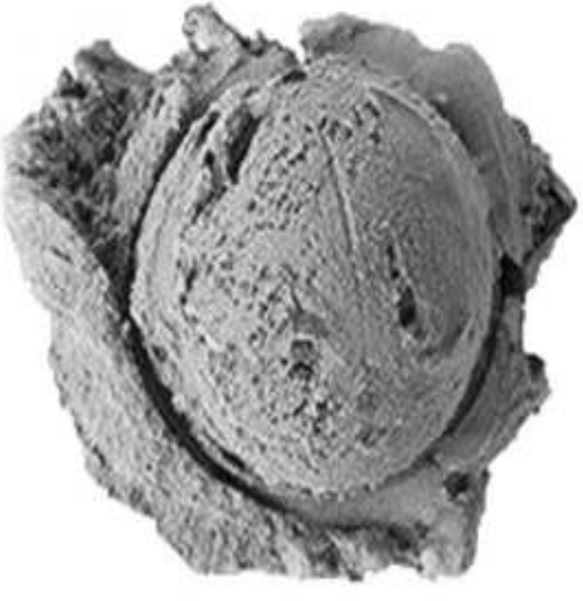
Monellin

- Monellin is a natural sweetener that is approx 1,500 times as sweet as sugar. It is found in the fruit of the Serendipity Berry which is native to Central and West Africa.
- **Uses:**
  Other than local consumption by natives in Africa it has not yet found use as a food, sweetener or pharmaceutical.

- **Benefits:**
  Zero glycemic index.
- Very sweet.
- Suitable for diabetics.
- It is a natural product.
- **Production:**
  It can be produced from the Serendipity Berry, though at the present time, no really cost effective method has yet been discovered..
- **Approval:**
  Japan is the only country so far to have approved it.

PRODUCTS FROM SERENDIPITY BERRY:

- Ice Cream
- Sorbet
- Dipity Pops
- Cakes
- Frozen Cocktails
- Desserts
- Soft Serve
- Toppings



Carefully sourced, and 100% delicious

Inspired Flavours

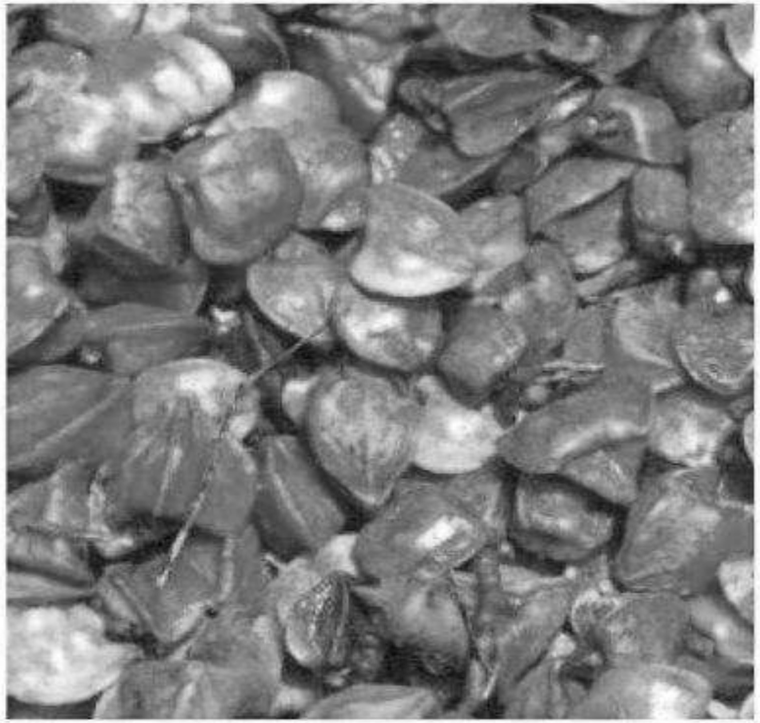
Trophies & medals for quality & taste

Made using 100% green energy

2. Katemfe

Thaumatin

- Thaumatin comes from the Katemfe Fruit which is native to Sudan and West Africa.



“Thaumatin Sweetner comes from the Katemfe Fruit in Africa. Many people have never heard about this miraculous fruit, and not much press has been given to the sweetener. This sweetener is very sweet, in the natural fruit state it has a slightly licorice taste, but when refined it’s very clean tasting.”

Benefits:

Zero glycemic index.

Very sweet. Not harmful to teeth.

Very suitable for diabetics. It is a natural product.

Production:

It is produced form wild Katemfe Fruit collected by locals from the rainforests of West Africa.

It is water extracted in a process that is said to be 100% natural.

Sold As:

Not sold on its own but usually as an ingredient to manufacturers of processed foods.

Talin is the brand name for one source.

Approval:

Approved in the United States.

3. LICORICE

Glycyrrhizin

- Glycyrrhizin is a natural sweetener that is extracted from licorice root. It is about 50 times as sweet as sugar.
- It has a strong licorice flavor and so is not suitable as a sweetener on its own. It have a zero glycemic index and is consequently suitable for diabetics.
- **Uses:**
  It has medicinal qualities and is used in the treatment of ulcers, and as an expectorant in cough mixtures.
- It is often used as an ingredient in toothpaste.
- It is heat resistant and can be used in cooking and processed food. It provides the sweetness in Sweet Chai Tea.
- It is sometimes used to provide flavor and sweeten tobacco.
- **Benefits:**
  It has a zero glycemic index and this makes it suitable as part of a diabetic diet. It does not contribute to tooth decay.
- It has medicinal qualities and is used in moderate amounts for a variety of ailments. It has even been shown to assist with the healing of burns.
- **Production:**
  It is extracted from the root of the licorice plant . Licorice is a member of the pea family that grows in warm climates.

4. Stevia

- The natural sweetener, alternative to saccharine and artificial sweeteners. Its high sweetening power and its zero calories make it a suitable complement for foods, in diabetic problems and in weight loss diets**.**
- **Chemical properties of Stevia:**
- Stevia leaves have a concentration of steviosides

Several researches have found that **stevia** has:

- Mineral content: Iron, manganessium and cobalt
- Molecular weight: 804
- It keeps its flavour stable under high and low temperatures.
- Stevia doesn’t ferment.
- It is soluble to water, alcohol.
- Calories: 0
- Saturated fat: 0
- Sugars: 0
- Cholesterol: 0
- Carbohydrates: 0

- **Steviosides**
- Stevioside is a mixture of 8 glycosides diterpenies, being the most stevioside and rebaudioside A the most relevant with 50% and 30% respectively.
- **Physical aspect**: Its crystals look like a fine powder of white ivory colour.
- **Sweetness**: It is the most relevant property. It has a sweetening power of more than 300 times that of saccharose.
- **Metabolism**: It does not metabolize in the body; therefore, it is not caloric and is suitable for diabetics.
- **Osmotic pressure**: low osmotic pressure.

This plant, known as stevia, is widely used nowadays. Japanese, Americans and many other consumers are using this plant as an **alternative sweetener in diabetic problems and in weight loss diets**, thanks to its absence of calories.

5. Gymnema sylvestre

- *Gymnema sylvestre* is an herb from India that has a long and varied history in traditional medicine, including its use as a:
- Diuretic
- Laxative
- Anti-inflammatory
- Circulatory system stimulant
- Diabetes treatment
- Weight loss aid

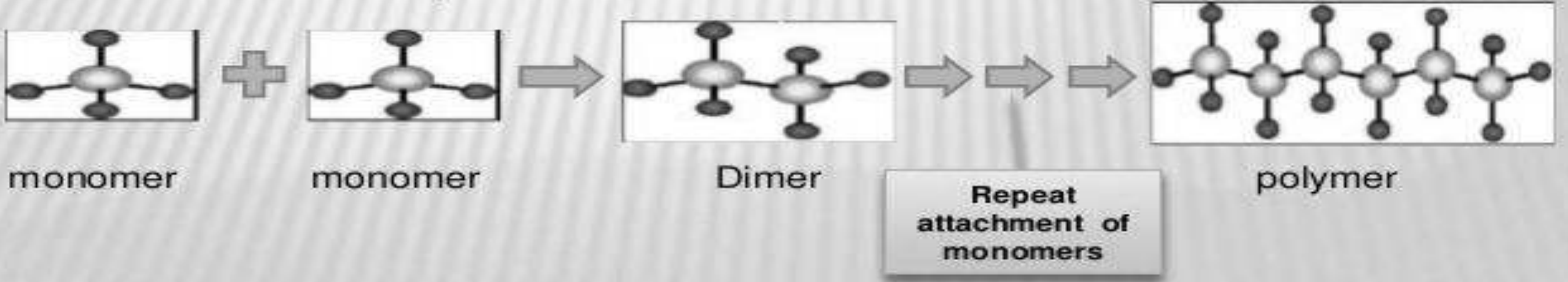
- *Gymnema sylvestre* appears to work by suppressing a desire for sugary foods as well as balancing blood sugar levels.
- The herb contains gymnemic acid, a nutrient found in certain plants that have been shown to suppress sweetness.
- Additionally, gymnemic acid is molecularly similar to glucose.
- The theory is that when you consume *Gymnema sylvestre*, it fills in your taste bud receptors, thereby preventing glucose from docking in those same receptors, thus cutting your craving for sugar and sweets.
- Similarly, because gymnemic acid is similar to glucose, *Gymnema sylvestre* may also lock into glucose receptors in your intestines, thereby preventing the absorption of sugar molecules. This would then lead to balanced blood sugar levels even when you consume sugar-based foods.

- *Gymnema sylvestre* significantly improves your ratio of HDL to LDL cholesterol, which is one of the most predictive indicators for developing heart disease.
- The herb also lowers triglycerides and "bad cholesterol."

C. NATURAL POLYMERS

INTRODUCTION

- A polymer is a large molecule (macromolecules) composed of many repeated subunits, known as monomers.
- Natural polymers and their derivatives are commonly used in medicine and pharmacy.
- Particular attention has recently been paid to natural polymers, because they are biocompatiable and biodegradable, so they can be hydrolyzed into removable and non-toxic products.

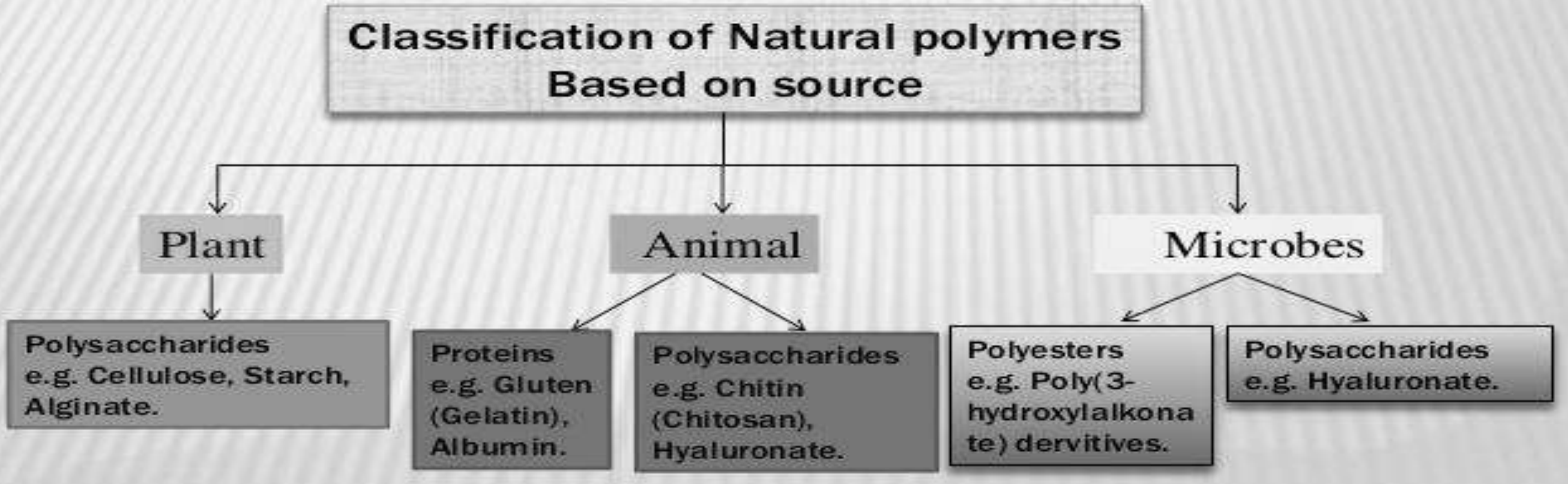


DEFINITION

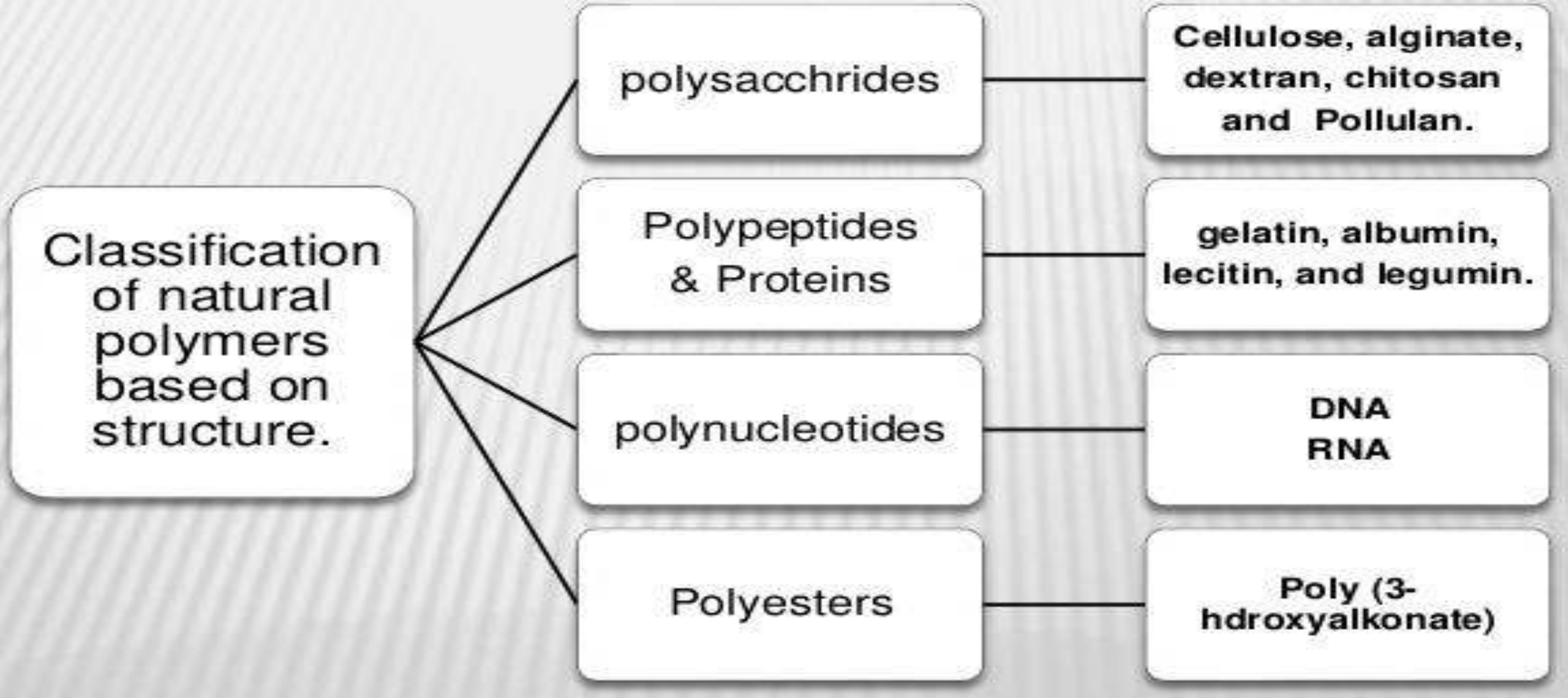
- The natural polymer is produced by living organisms and result from only raw materials that are found in nature.

CLASSIFICATION

- The natural polymers are classified based on source or structure.

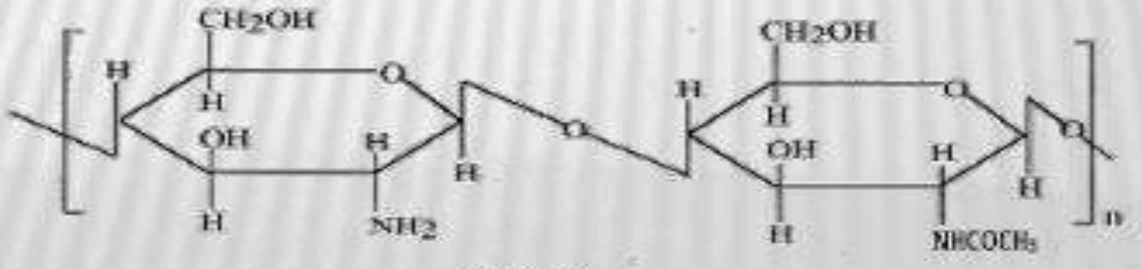


CLASSIFICATION



CHITOSAN:

- Introduction:
  - Chitin is a macromolecule found in the shells of crabs, lobsters, shrimps and insects
  - Chitosan is obtained by partial deacetylation of chitin.
  - Chitin is insoluble in its native form but chitosan, the partly deacetylated form, is water soluble.
- Chemistry:
  - linear co-polymer of β(1-4) linked glucosamine and N-acetyl-D-glucosamine.



Chitosan

PHYSIOCHEMICAL PROPERTIES

- Odorless, white or creamy-white powder
- Chelates many transitional metal ions
- Highly basic polysacharides
- in acidic pH, it gets solubilized due to protonation of free amino groups and the resultant soluble polysaccharide is positively charged.
- hydrophilic in nature thereby it has the ability to form gels at acidic pH.
- Degraded by lysozyme to it's by products glucosamine and n-acetyl glucosamine

APPLICATION

- Ocular delivery:
  - making contact lens- optical clarity, sufficient optical correction, gas permeability, particularly towards oxygen, wettability and immunological compatibility.
  - antimicrobial and wound healing properties of chitosan along with an excellent film capability make chitosan suitable for development of ocular bandage lenses.
- Colon drug delivery:
  - Degraded by microflora present in human colon which supports colon drug delivery
- Coating material:
  - Good film forming property and mucoadhesive property

- Mucosal delivery:
  - Chitosan gets protonated in acidic solution, so it binds strongly to negatively charged cell surface making it useful to formulate bioadhesive dosage forms.
- Transdermal drug delivery:
  - Studies on propranolol hydrochloride (prop-HCl) delivery systems using various chitosan membranes with different crosslink densities as drug release controlling membranes and chitosan gel as the drug reservoir have been performed.
- Gene Delivery:
  - Chitosan, typically isolated from the shell of shrimp, has the ability to react with DNA and compact it to produce a nanoparticle. Such nanoparticles are more readily taken up by cells.

GELATIN:

- INTRODUCTION
  - Gelatin is a natural water soluble functional polymer (protein) that is derived by partial hydrolysis of collagen (chief protein component in skin, bones and white connective tissues of the animal body).
  - It is commonly used for pharmaceutical and medical applications because of its biodegradability and biocompatibility in physiological environments.
- GELATIN TYPES
  - Gelatin derived from an acid-treated precursor is known as Type-A and gelatin derived from an alkali-treated process is known as Type-B.
  - Results in a difference in isoelectric points (IP), being 7 – 9 for gelatin type A and 4 – 5 for gelatin type B.

MFG OF GELATIN

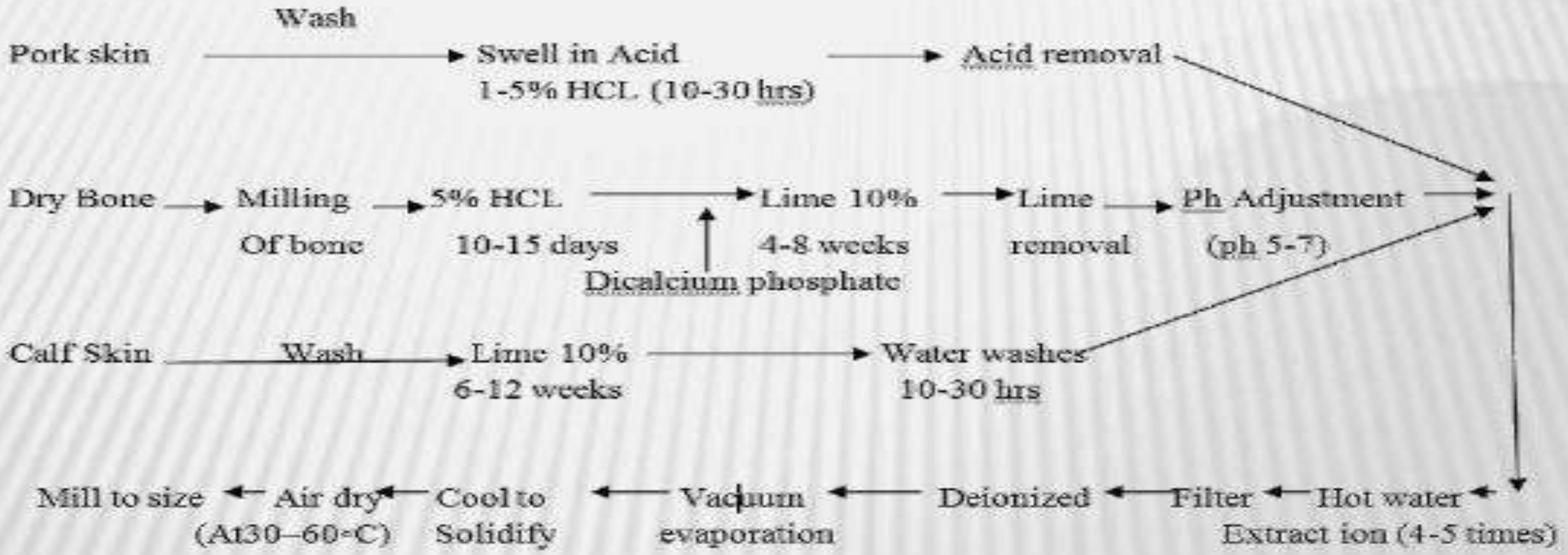


Fig.: Flow chart explaining extraction process of Gelatin

PHYSICOCHEMICAL PROPERTIES

- Formation of thermo-reversible gels in water: When gelatin granules are soaked in cold water they hydrate into discrete, swollen particles. On being warmed, these swollen particles dissolve to form a solution.
- Soluble in aqueous solutions of polyhydric alcohols such as glycerol and propylene glycol.
- Insoluble in less polar organic solvents such as benzene, acetone, primary alcohols and dimethylformamide.
- Gelatin stored in air-tight containers at room temperature remains unchanged for long periods of time. When dry gelatin is heated above 45° C in air at relatively high humidity (above 60% RH) it gradually loses its ability to swell and dissolve.
- Sterile solutions of gelatin when stored cold are stable indefinitely; but at elevated temperatures the solutions are susceptible to hydrolysis.
- Gelatin is composed of 50.5% carbon, 6.8% hydrogen, 17% nitrogen and 25.2% oxygen. It gives typical protein reactions and is hydrolyzed by most proteolytic enzymes to yield its peptide or amino acid components.

APPLICATION

- Two-Piece Hard Capsules
- Soft Elastic Gelatin Capsules
- As a binder in Tablet
- Tablet Coating
- Suppositories
- Gelatin Emulsions
- Microencapsulation
- Source of essential amino acids
- Absorbable Gelatin Sponge
- Gelatin as Nanoparticle and microparticles.

Gums are considered to be pathological products formed following injury to the plant or owing to unfavorable conditions, such as drought, by a breakdown of cell walls (extra cellular formation; gummosis) while, mucilages are generally normal products of metabolism, formed within the cell (intracellular formation) and/or are produced without injury to the plant. Gums readily dissolve in water, whereas, mucilage form slimy masses. Gums are pathological products, whereas mucilages are physiological products.

Acacia, tragacanth, and guar gum are examples of gums while mucilages are often found in different parts of plants. For example, in the epidermal cells of leaves (senna), in seed coats (linseed, psyllium), roots (marshmallow), barks (slippery elm) and middle lamella (aloe).

Advantages:

1.Biodegradable—naturally available biodegradable polymers are produced by all living organisms. They represent truly renewable source and they have no adverse impact on humans or environmental health (e.g., skin and eye irritation).

2.Biocompatible and nontoxic—chemically, nearly all of these plant materials are carbohydrates composed of repeating sugar (monosaccharides) units. Hence, they are non3 toxic.

3.Low cost—it is always cheaper to use natural sources. The production cost is also much lower as compared with that for synthetic material.

4.Environmental3friendly processing—gums and mucilages from different sources are easily collected in different seasons in large quantities due to the simple production processes involved.

THANK U

Pharmaceutical Validation

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Pravara Rural College of Pharmacy, Pravaranagar

What is Validation?

- The goal of validation is to:

  "establish documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes."

  In simple terms- Validation is the documented act of proving that any procedure, process, equipment, material, activity or system actually leads to the expected result.

What is Validation?

- What does this mean?
  - An quantitative approach is needed to prove quality, functionality, and performance of a pharmaceutical/biotechnological manufacturing process.
  - This approach will be applied to individual pieces of equipment as well as the manufacturing process as a whole.
  - The validation process is regulated by the guidelines and restrictions set forth by the FDA. However, the actual validation protocol, documentation, and execution is the responsibility of the manufacturer.

Validation studies

- Analytical test
- Equipment
- Facility systems / Process (air, water, steam, process; manufacturing processes, cleaning, sterilization, sterile filling, lyophilization)

Validation studies

- verify the system under test under the extremes expected during the process to prove that the system remains in control.
- Critical equipment and processes are routinely revalidated at appropriate intervals to demonstrate that the process remains in control.

Type of validation

- Prospective : pre-planned protocol
- Concurrent
- Retrospective

Phases of Validation

- Phases of Validation
  - Validation is broken down into three phases:
    - Installation Qualification (IQ)
    - Operational Qualification (OQ)
    - Performance Qualification (PQ)
  - These three protocols are used to define tests that will demonstrate that the process consistently and repeatedly produces the desired product.

Phases of Validation

- Installation Qualification (IQ)
  - This is the first step in validation.
  - This protocol insures that the system/equipment and its components are installed correctly and work in accordance with established specifications.
  - Calibration of major equipment, accessory equipment, and/or utilities should be performed in this step as well.

Phases of validation

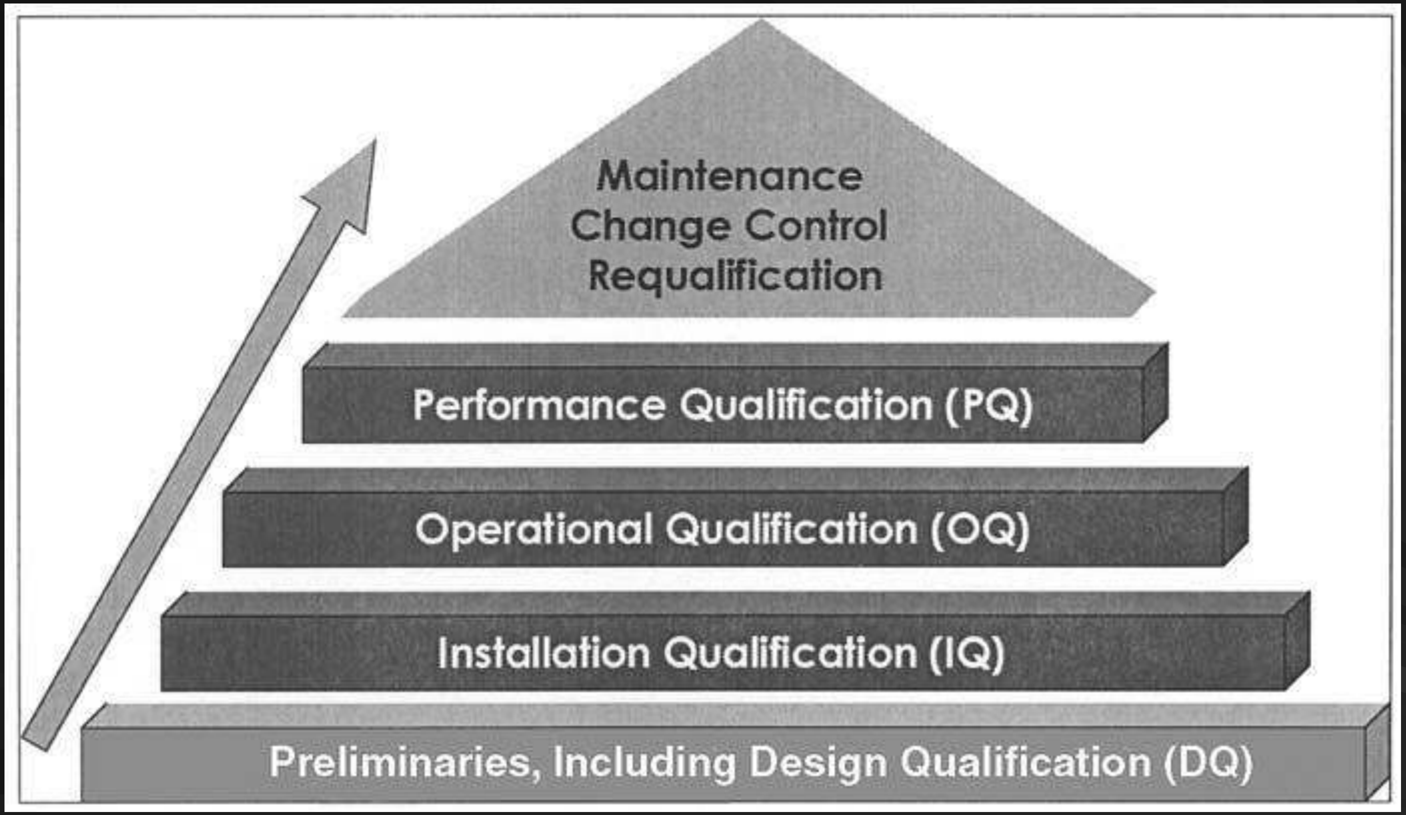
- Operational Qualification (OQ)
  - This step proceeds after the IQ has been performed.
  - In the OQ, tests are performed on the critical parameters of the system/process.

- Documented verification that the system or sub-system performs as intended throughout all anticipated operating ranges. Operational qualification tests whether or not the system works as expected.

Phases of validation

- Performance Qualification (PQ)
  - This is the third and final phase of validation.
  - This phase tests the ability of the process to perform over long periods of time within tolerance deemed acceptable.
  - PQ is performed on the manufacturing process as a whole. Individual components of the system are not tested individually.

Phases of validation



Equipment Validation

- As mentioned earlier, each piece of equipment must be validated in order to legally operate within the facility.
- The goal is to produce consistent results with minimal variation without compromising the integrity of the product and the persons operating the equipment.
- A plan of validation should be drafted and executed in order to satisfy guidelines. The validation plan generally consists of IQ and OQ sections.
- Any major equipment changes after the initial validation will result in the need for subsequent revalidation.
- In the end, equipment validation will create specification ranges and tolerances that will be applied to the normal operation of equipment.

Process Validation

- The manufacturing process, in addition to the individual equipment, must be validated.
- A process is a series of interrelated functions and activities using a variety of specified actions and EQ which is designed to produce a defined result/ product.
- The goal is to create a robust manufacturing process that consistently produces a drug product with minimal variation that adheres to quality criteria of purity, identity, and potency.
- A validation plan for the manufacturing process should be drafted and executed in order to satisfy guidelines. The validation plan usually involves just a PQ section.

Process Validation

- Just as equipment validation, major changes after the initial validation will result in the need for subsequent revalidation.
- In the end, process validation will ensure a robust product that is highly reproducible over time.

Process validation studies

- examine a process under normal operating conditions to prove that the process is in control
- re-validation
  – modification to the process
  – problems occur
  – EQ or systems are changed

Process validation

- To validate the reproducibility and consistency of a process
  - full defined process is carried out using validated EQ
  - at least 3 times, under established procedure
  - process must successfully and consistently meet all acceptance criteria at all steps throughout the procedure at least 3 times consecutively

Validated process

Worst case: to ensure that process is acceptable in the extreme case

Process validation

- Example
  - cleaning
  - sanitization
  - fumigation
  - depyrogenation
  - sterilization
  - sterile filling
  - fermentation
  - bulk production
  - purification
  - inactivation
  - filling, capping, sealing
  - lyophilization

A Typical Validation Plan

1. Introduction
2. Installation qualification
   a. Facilities
   b. Utilities
   c. Equipment
3. Operation qualification
   Testing protocols for utilities and equipment
4. Validation
   Testing protocols for products and cleaning systems
5. Documentation
6. Validation of the QA testing laboratory
7. SOPs
8. Training of personnel
9. Organization charts
10. Schedule of events

Validation: Type of Documentation

- Validation master plan (VMP)
- Validation protocol (VP)
- Validation reports (VR)
- Standard operating procedures (SOPs)

Master validation plan (MVP)

- is a document pertaining to the whole facility that describes which EQ, systems, methods and processes will be validated and when they will be validated.
- provide the format required for each particular validation document (IQ, OQ, PQ for EQ and systems; process validation, analytical assay validation)

Master validation plan (MVP)

- indicate what information is to be contained within each document
- indicate why and when revalidations will be performed
- who will decide what validations will be performed
- order in which each part of the facility is validated
- indicate how to deal with any deviations
- state the time interval permitted between each validation
- Enables overview of entire validation project
- List items to be validated with planning schedule as its heart
- like a map

Validation: In summary, VMP should contain at least

- Validation policy
- Organizational structure
- Summary of facilities, systems, equipment, processes to be validated
- Documentation format for protocols and reports
- Planning and scheduling
- Change control
- Training requirements

Validation: Protocol

- Objectives of the validation and qualification study
- Site of the study
- Responsible personnel
- Description of the equipment
- SOPs
- Standards
- Criteria for the relevant products and processes

Validation: Report

- Title
- objective of the study
- Refer to the protocol
- Details of material
- Equipment
- Programmes and cycles use
- Details of procedures and test methods

Validation: changes that require revalidation

- Software changes; controllers
- Site changes; operational changes
- Change of source of material
- Change in the process
- Significant equipment changes
- Production area changes
- Support system changes

Resources

- www.validationworld.com
  - Information concerning IQ: http://www.cqionline.com/knowledge/iq.html
  - Information concerning OQ: http://www.cqionline.com/knowledge/oq.html
  - Information concerning PQ: http://www.cqionline.com/knowledge/pq.html
- Patricia Stewart-Flaherty. Performance Validation. Presentation. 13 Apr. 2003.
- Sofer, Gail and Zabriskie, Dane W., ed. <u>Biopharmaceutical Process Validation</u>. New York: Marcel Dekker, 2000.
- Avis, Kenneth E., Wagner, Carmen M., Wu, Vincent L., ed. <u>Biotechnology: Quality Assurance and Validation</u>. Buffalo Grove, Illinois: Interpharm Press, Inc., 1999.
- Carleton, Fredrick J. and Agalloco James P. ed. <u>Validation of Pharmaceutical Processes</u>. New York: Marcel Dekker, Inc., 1999.

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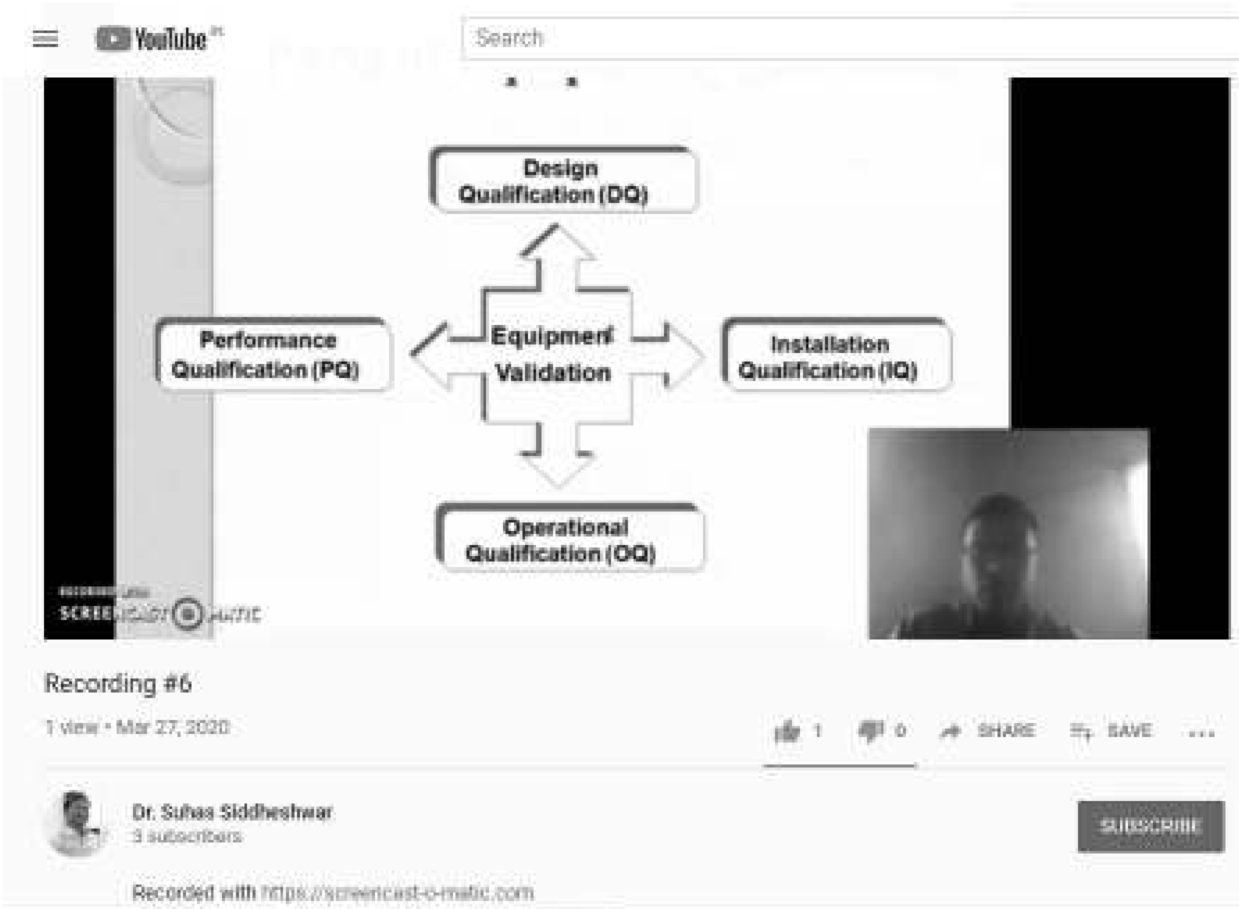

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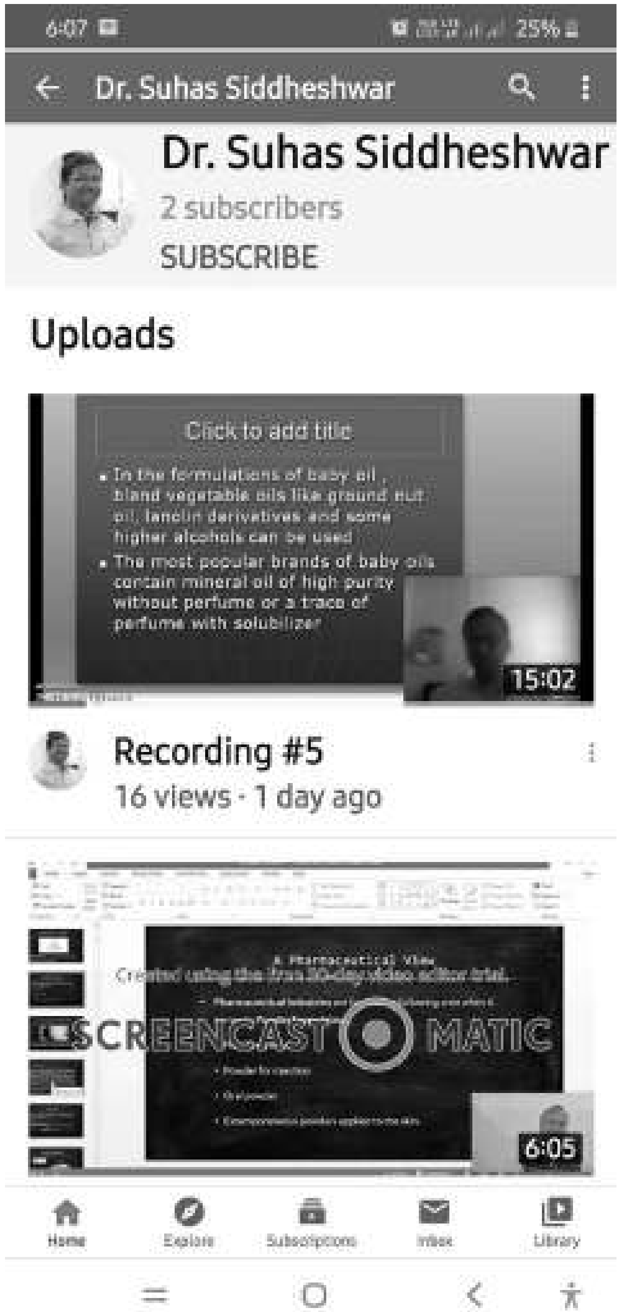

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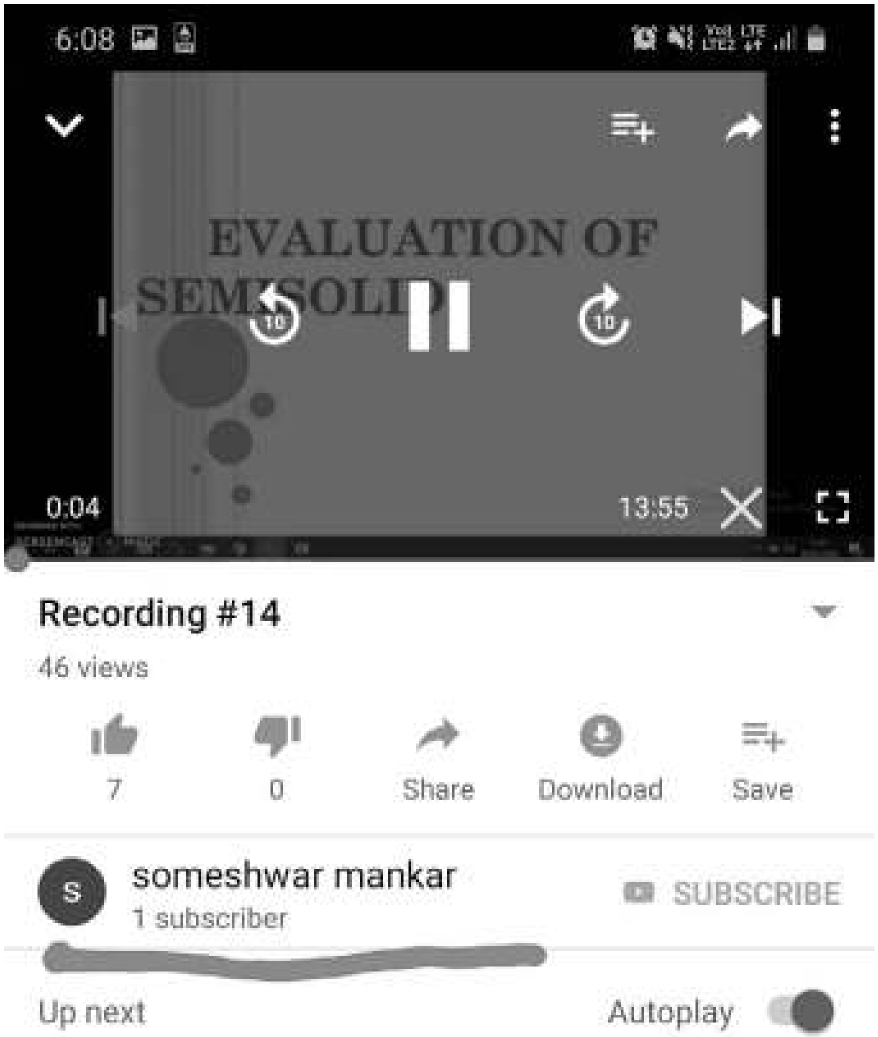

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ZOOM VIDEOCONFERENCING

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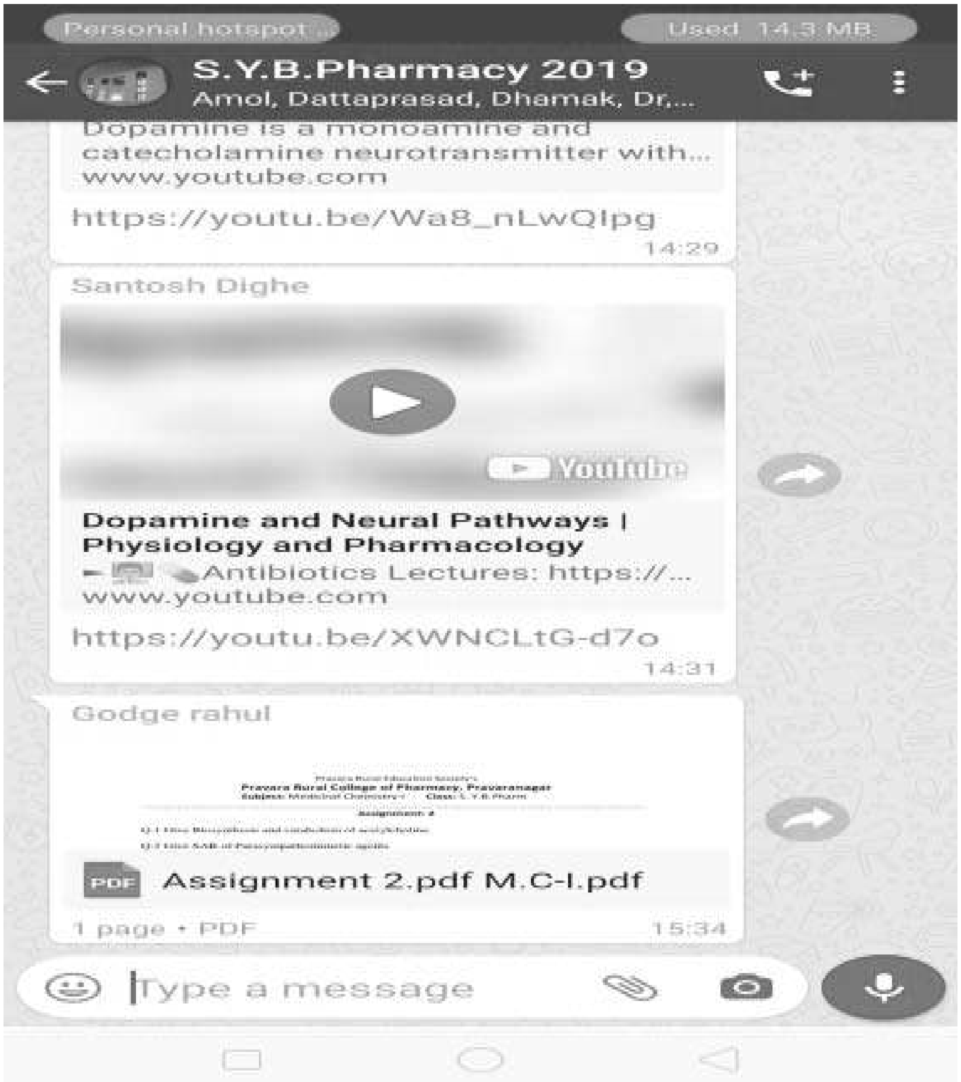

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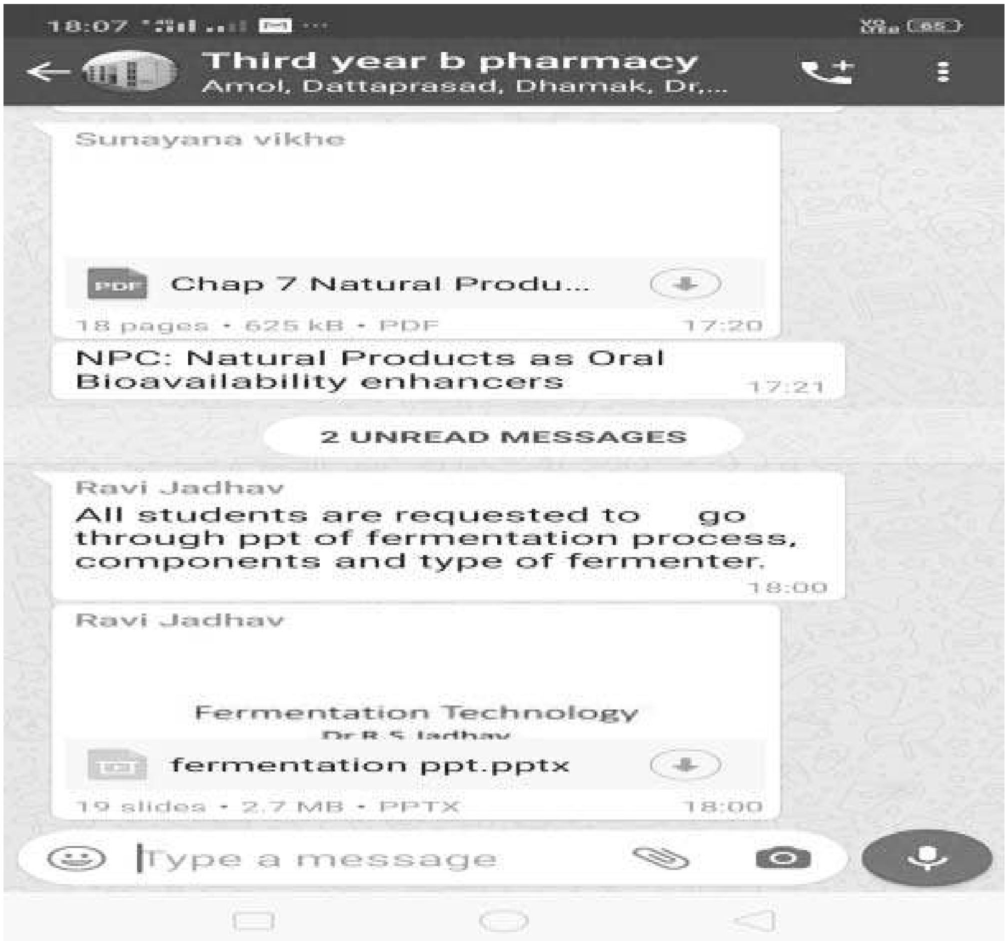

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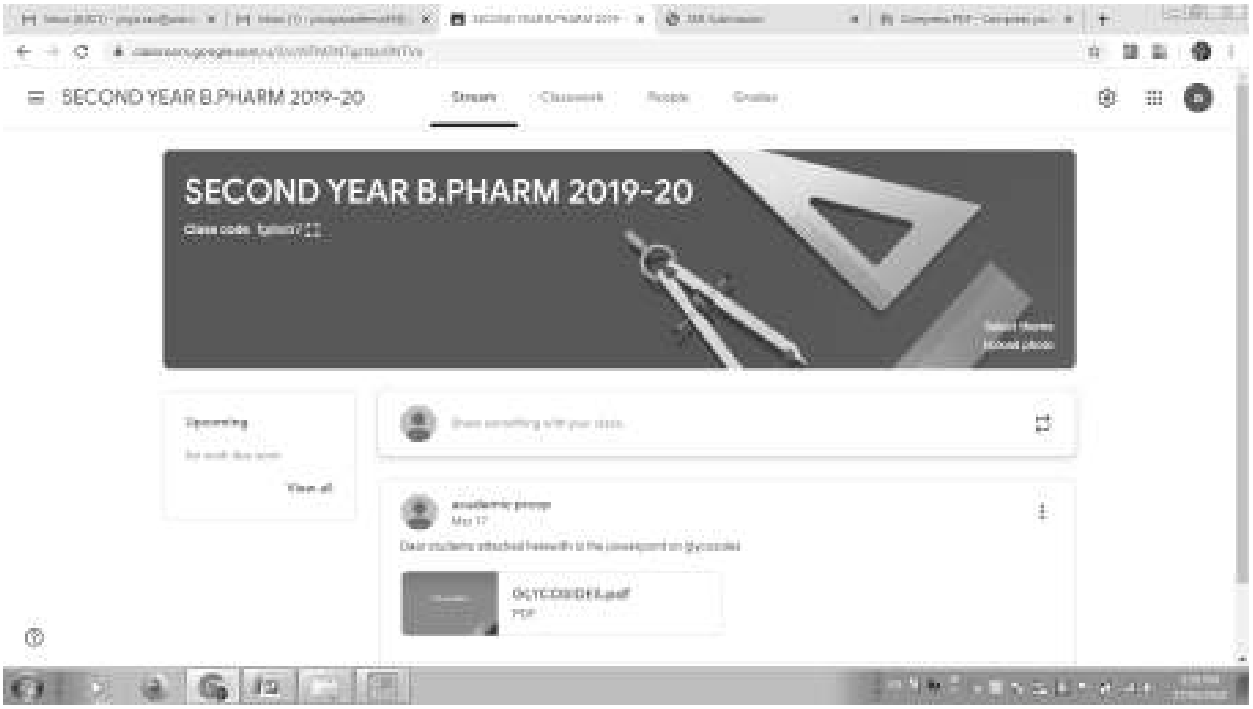

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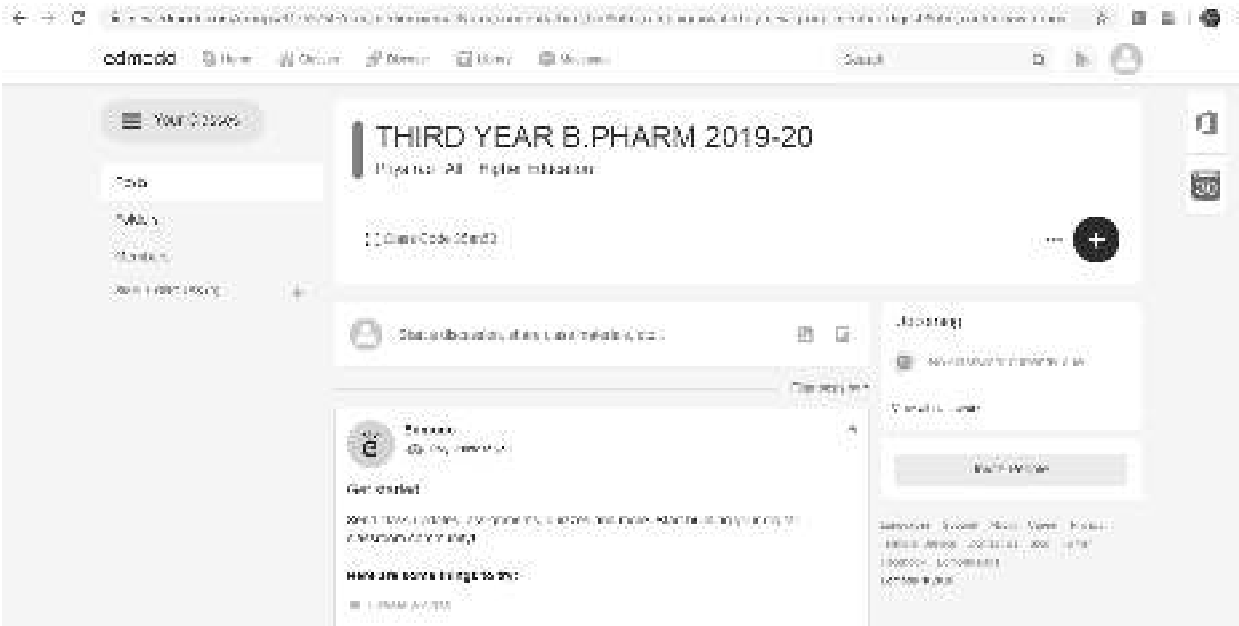

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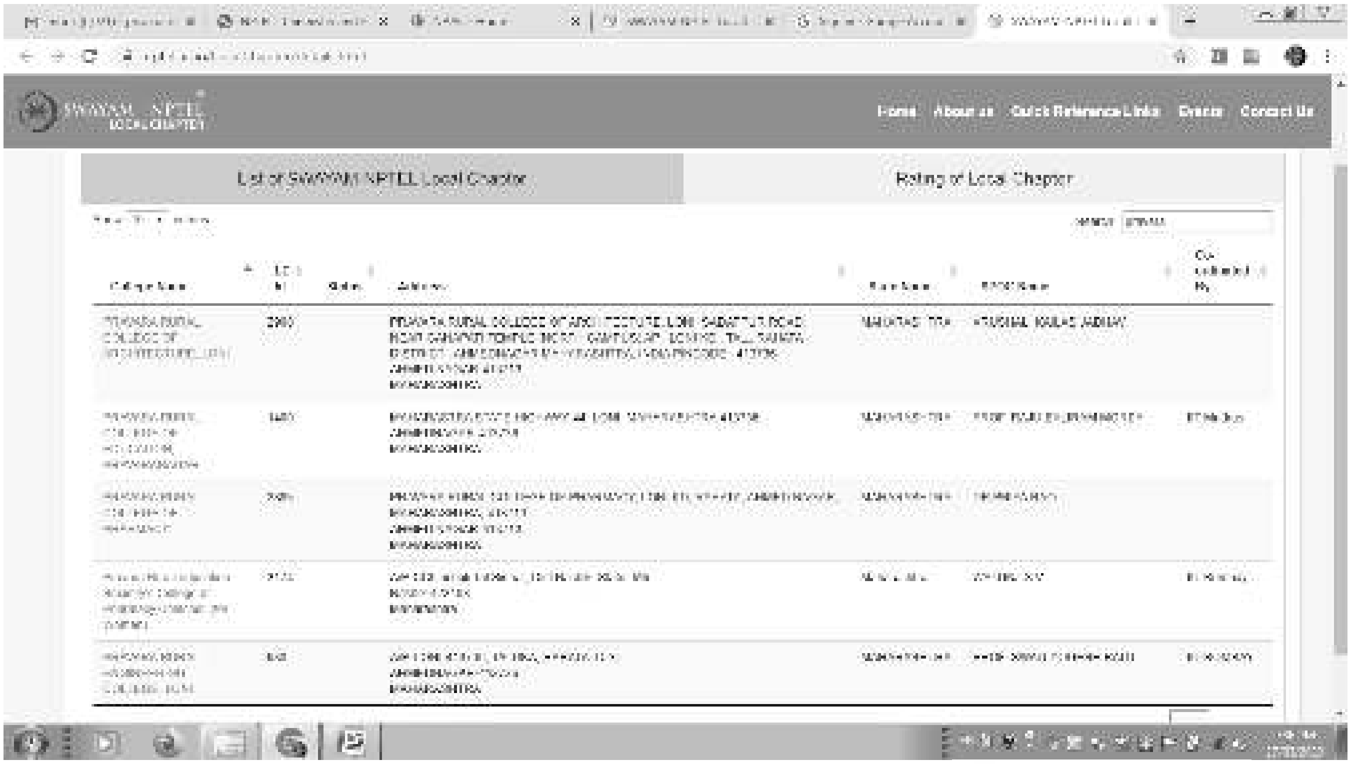
NPTEL LOCAL CHAPTER



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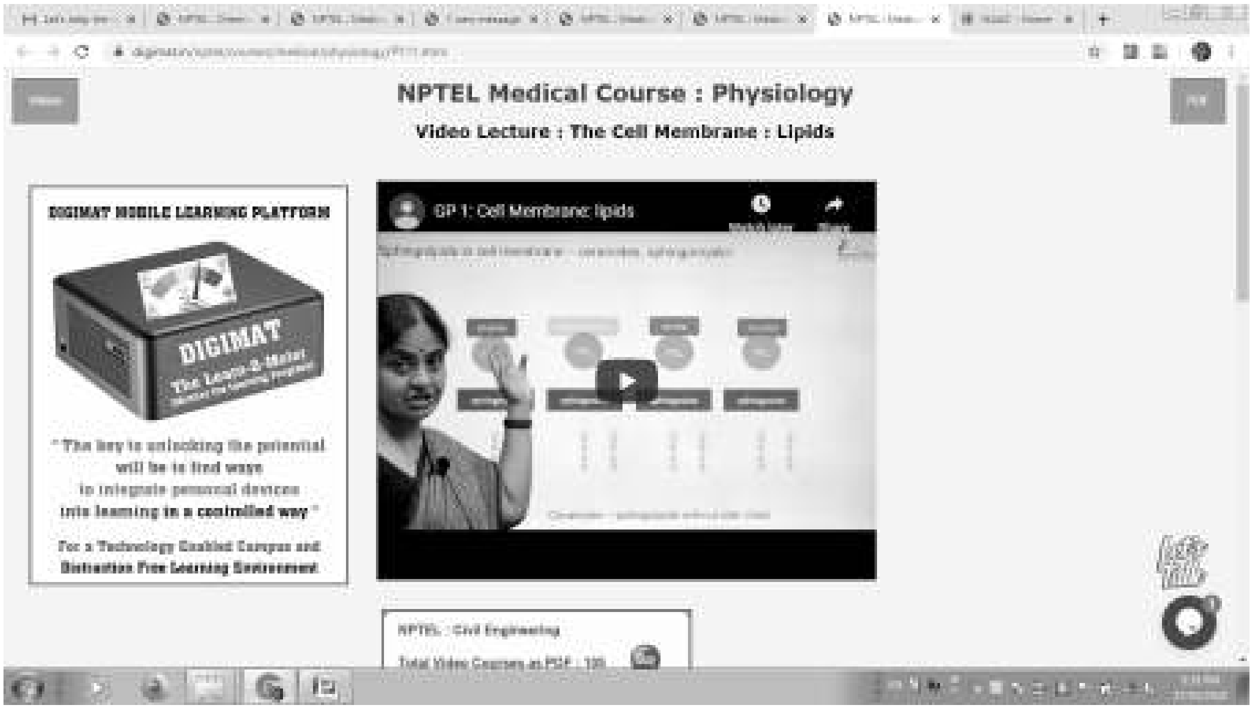
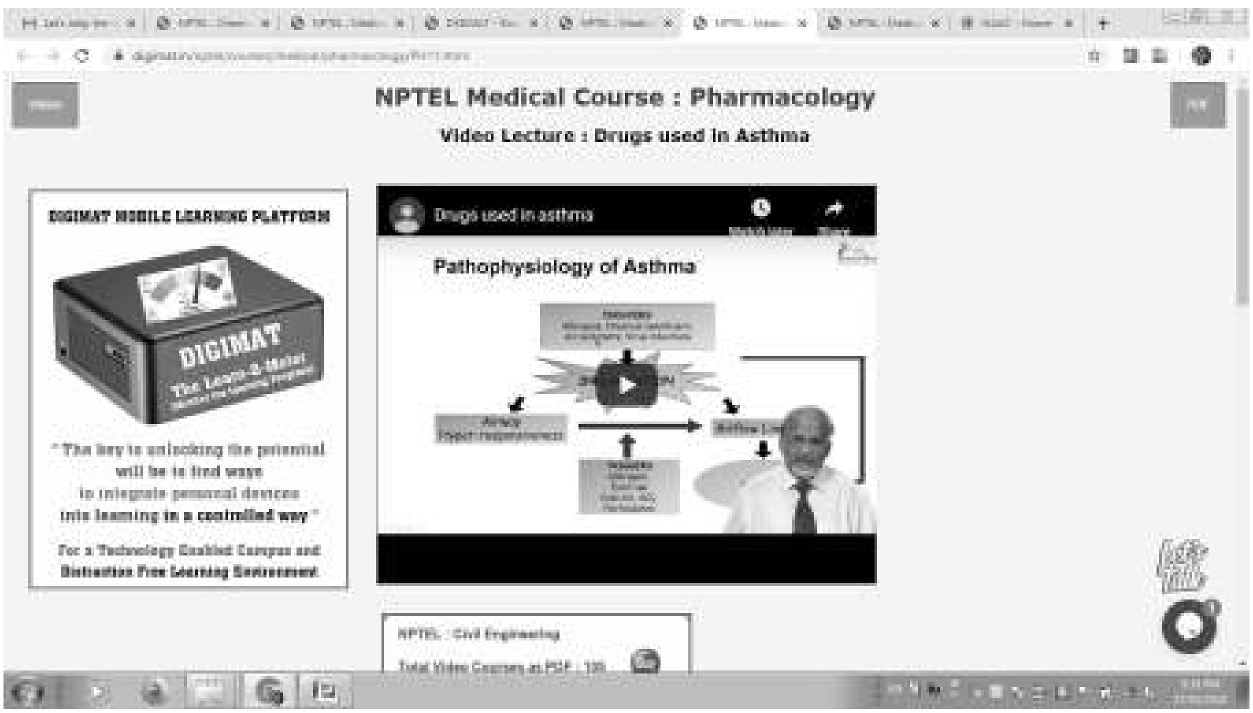
USE OF NPTEL VIDEOS





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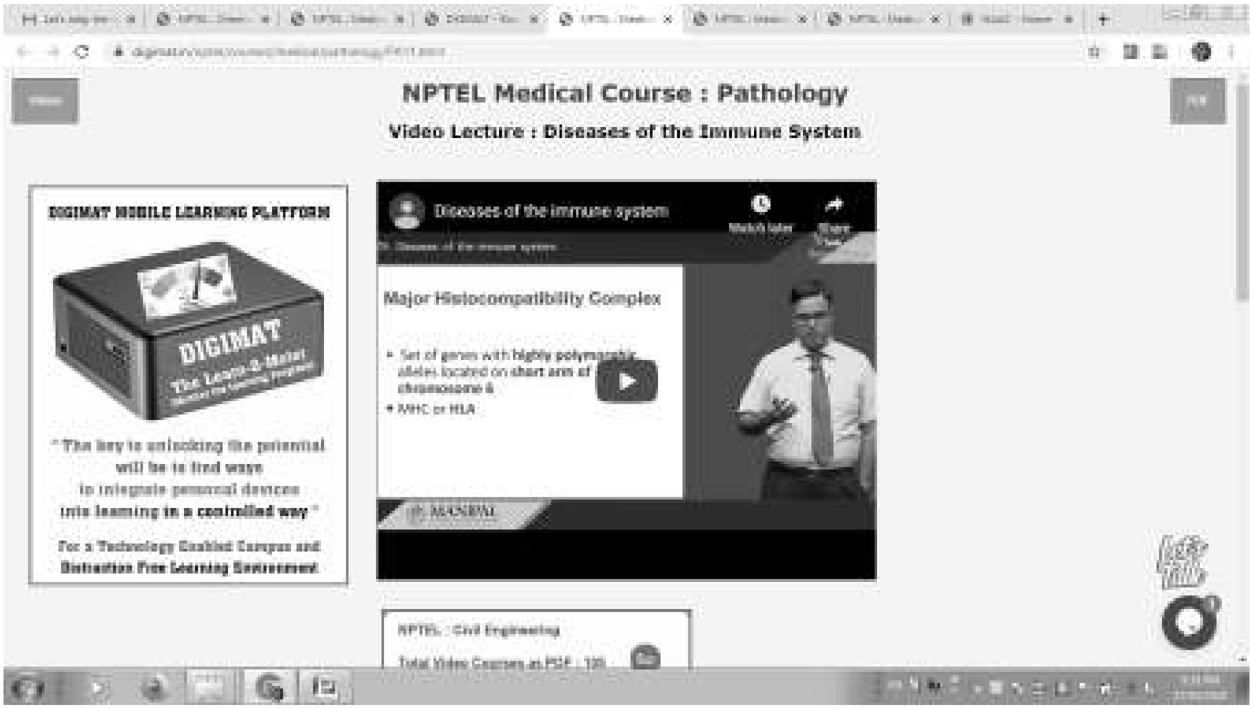

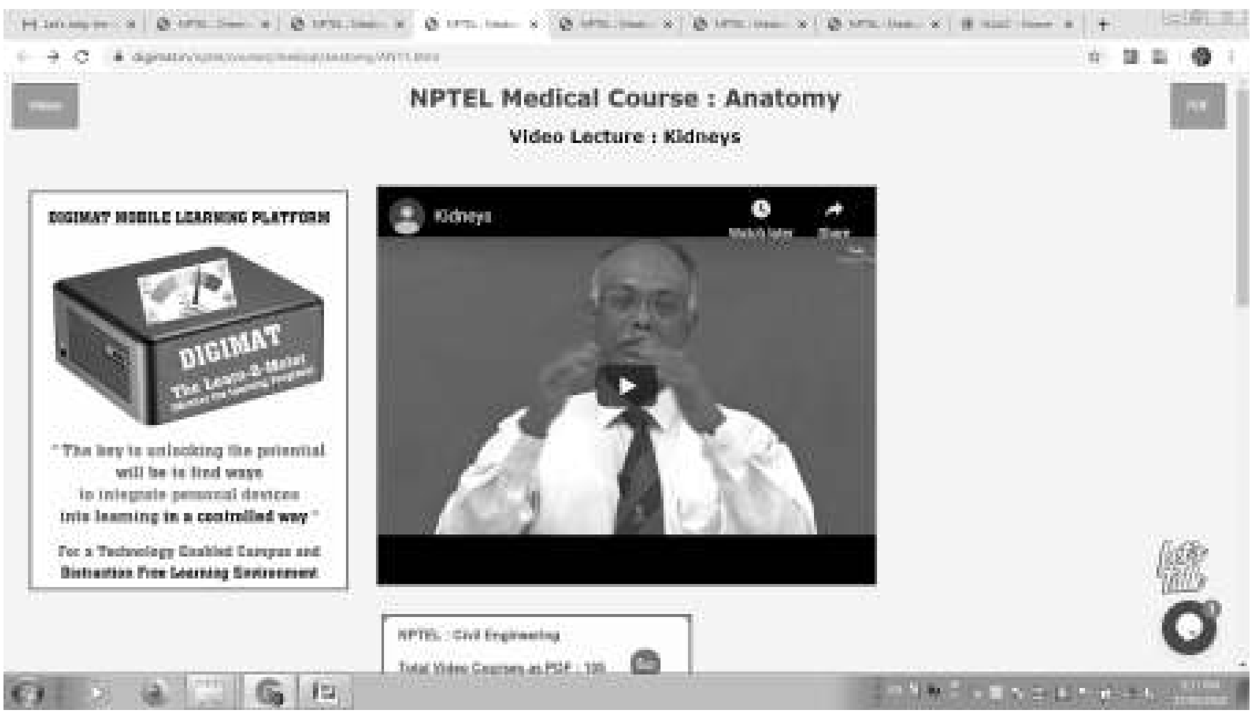

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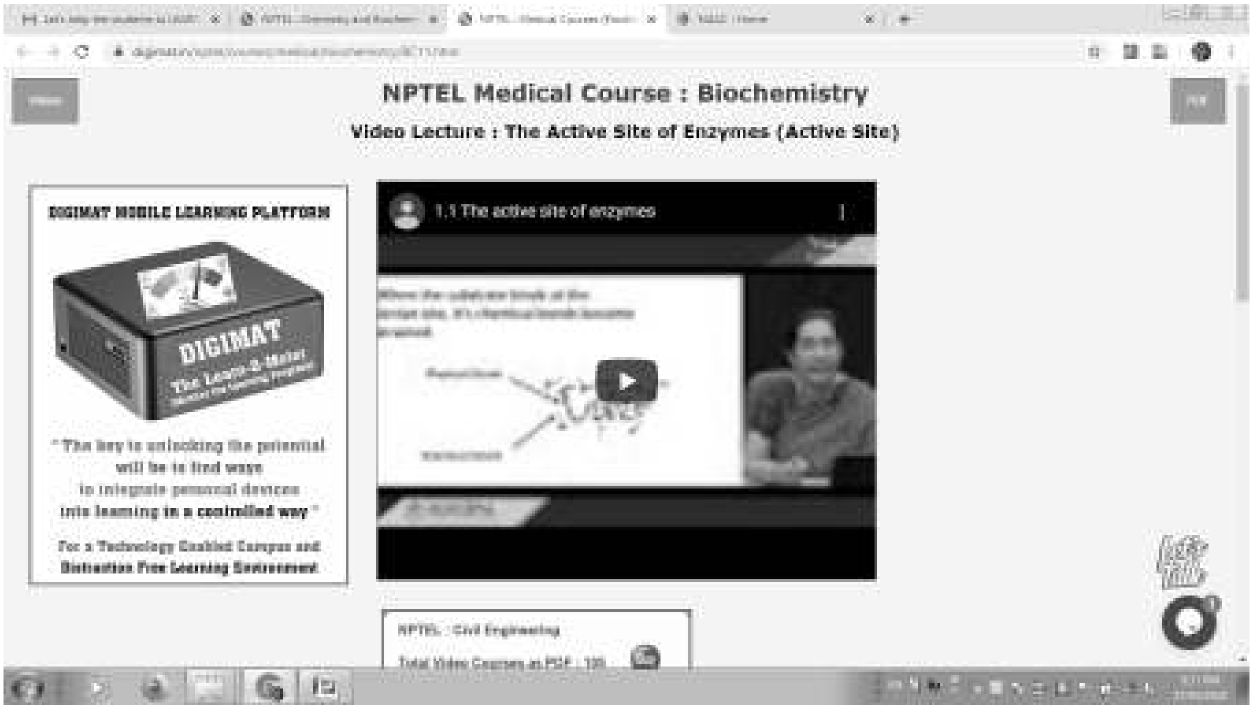
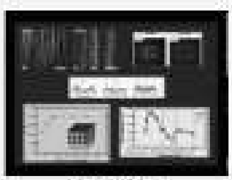
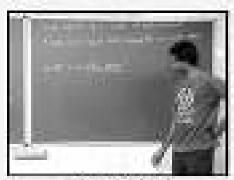
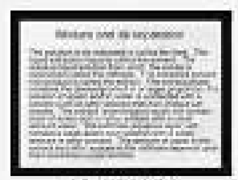
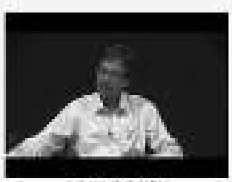


Chemistry of Materials	Mathematics for Chemistry	Advance Analytical Course
 104104011	 104104026	 104104066
Bio-inorganic chemistry	Rate processes	Heterocyclic Chemistry
 104105031	 104105041	 104105034
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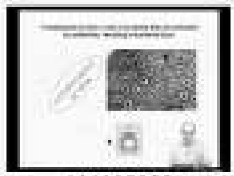
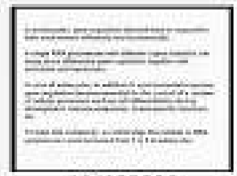
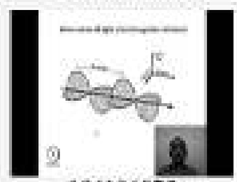
Principles and Applications of Electron Paramagnetic Resonance Spectroscopy  104106048	Essentials in Immunolgy  104108055	Eukaryotic Gene Expression - basics and benefits  104108056
Introductory Quantum Chemistry  104108057	Introduction to Organometallic Chemistry  104108062	NOC:Chemistry - I  104106072
Bio-Chemistry I  102105034	NOC:Biochemistry  104105076	NOC:Application of Spectro-scopic Methods in Molecular Structure Determination  104106075

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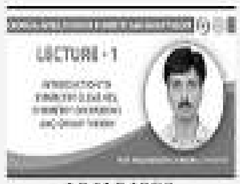
NOC:Organo Metallic Chemistry  104101079	NOC:Chemical Applications of Symmetry and Group Theory  104104080	NOC:Chemistry I:Introduction To Quantum Chemistry And Molecular Spectroscopy  104106083
NOC:Quantum Computing  104104082	NOC:Mathematics for Chemistry  104104081	NOC:Basics of Fluroscence Spectroscopy  104104084

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NOC:Introduction To Molecular Thermodynamics  104105088	NOC:Chemistry Of Main Group Elements  104101090	NOC:Transition Metal Organometallic Chemistry: Principles to Applications  104101091
NOC:A Study Guide In Organic Retrosynthesis: Problem Solving Approach  104105087	NOC:Introduction to Chemical Thermodynamics and Kinetics  104106089	NOC:Inorganic Chemistry of Life: Principles and Perspectives  104101093

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NOC:Chemical Crystallography

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NOC:Advanced Chemical Thermodynamics and Kinetics

104106094

NOC:Chemistry: Atomic Structure and Chemical Bonding

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NOC:Molecular Spectroscopy: A Physical Chemists Perspective

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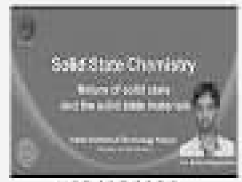
NOC:Advanced Transition Metal Organometallic Chemistry

104101100

NOC:Solid State Chemistry



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NOC:Experimental Biochemistry

104105102

NOC:Industrial Inorganic Chemistry

104105103

NOC:Reactive Intermediates Carbene and Nitrene

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NOC:Electrochemical Impedance Spectroscopy  104106105	NOC:Medicinal Chemistry  104106106	NOC:Chemical Principles-II  104106107
NOC:Multidimensional NMR Spectroscopy for Structural Studies of Biomolecules  104108097	NOC:Symmetry and Structure in the Solid State  104108098	Organic Chemistry Lab Certification  104106108
NOC:Mechanisms in Organic Chemistry  104101115	NOC:Metals In Biology  104101116	NOC:NMR spectroscopy for Chemists and Biologists  104101117

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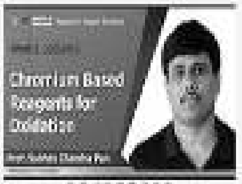
NOC:Reagents In Organic Synthesis



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NOC:Thermodynamics: Classical to statistical

104103112

NOC:Bioinorganic Chemistry

104104109

NOC:Organic Chemistry in Biology and Drug Development

104105120

NOC:Introductory Organic Chemistry I

104106119

NOC:Ultrafast Optics and Spectroscopy

104108118

Bio-Physical Chemistry

104102009

NOC:Basics in Inorganic Chemistry

104101121

NOC:Ultrafast Laser Spectroscopy

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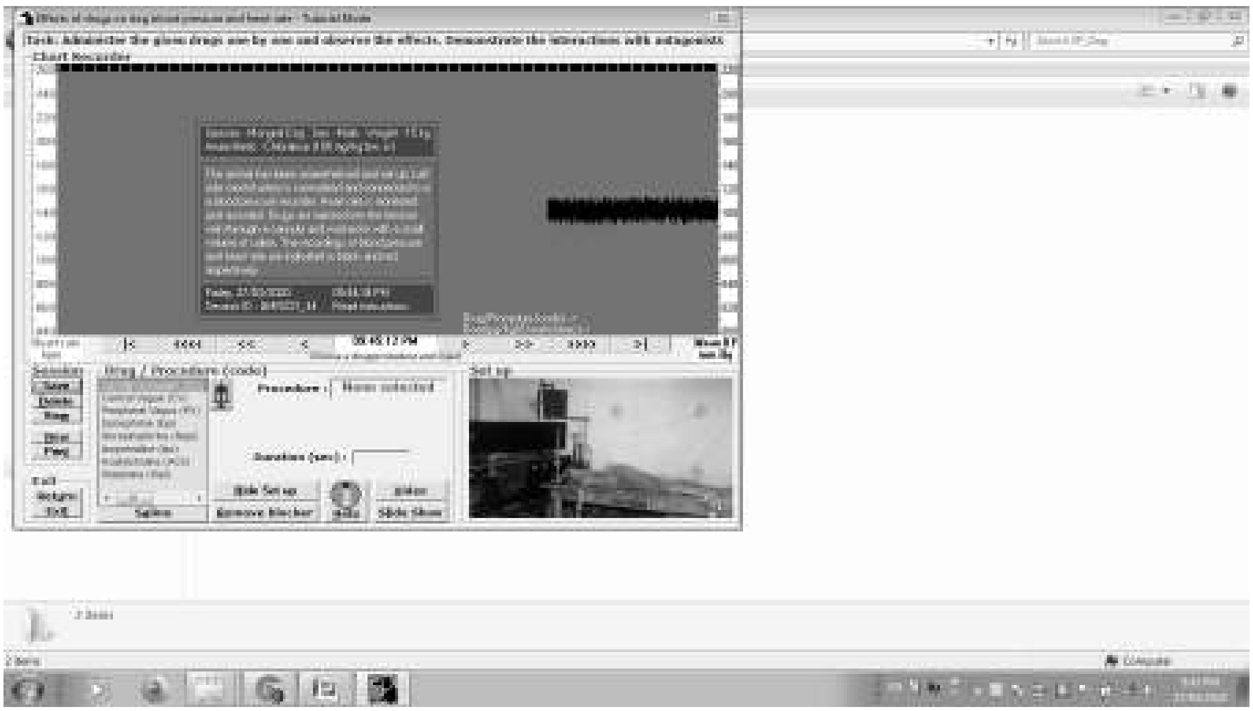
SOFTWARE FOR ANIMAL EXPERIMENTATION

DOG EXPERIMENT



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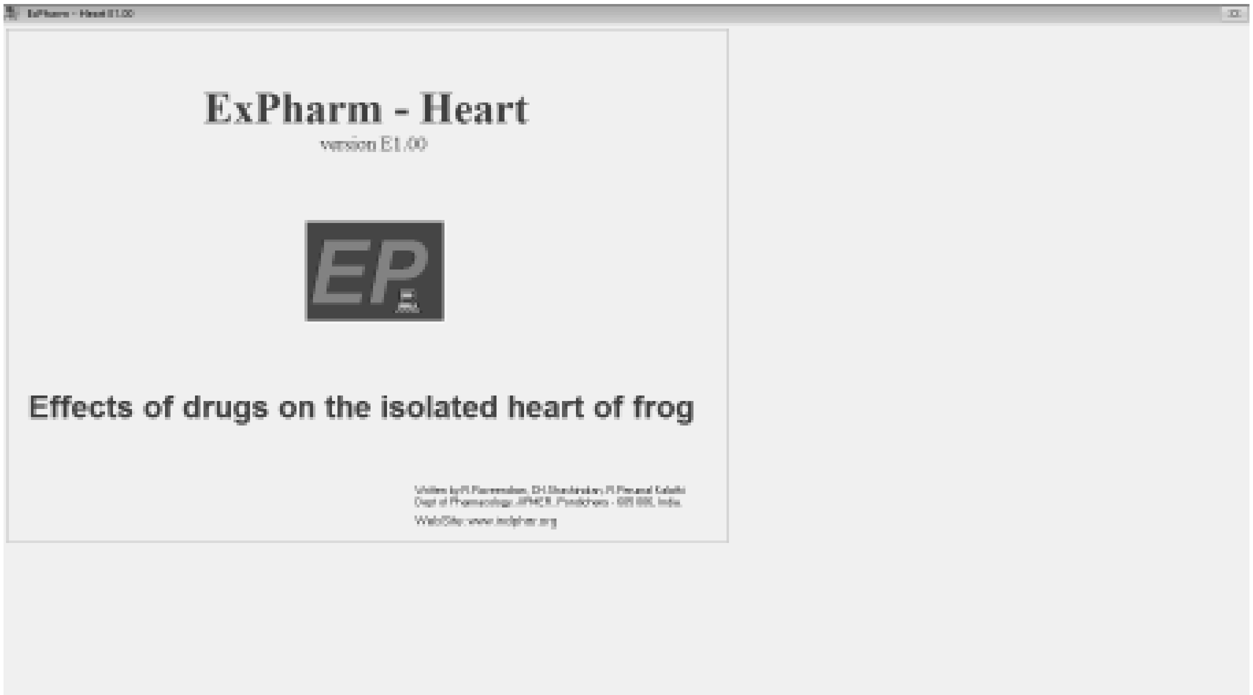
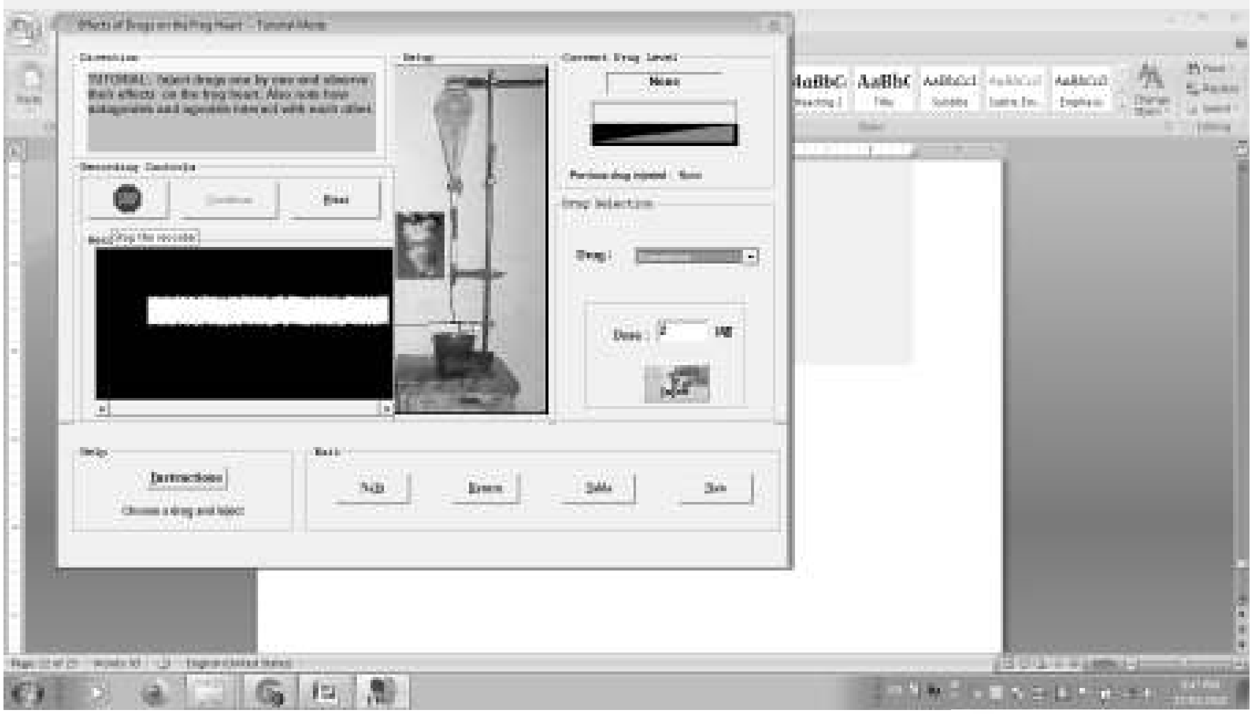
EFFECT OF DRUGS ON ISOLATED HEART OF FROG





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