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FORMULATION AND EVALUATION OF TRANSDERMAL PATCH CONTAINING NATURAL RELEASE RETARDANT

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1.1 INTRODUCTION: - SKIN

Skin is the largest organ of body, accounting for about 15% of total adult body weight. it perform many vital functions, including protection against external physical, chemical and biologic assailants as well as prevention of excess water loss from body and role in thermoregulation.

The skin is continuous with the mucous membrane lining the body surface. The integumentary system is form by the skin and its derivative structure skin is composed of three layers the epidermis, dermis and subcutaneous tissue.

The outermost level consists of specific constellation of cells known as keratinocytes which function to which function to synthesize keratin, a long, threadlike protein with a protective role. The middle layer, the dermis, is fundamentally made up of the fibrillar structural protein known as collagen. The dermis lies on the subcutaneous tissue, or panniculus, which contains small lobesof fat cells known as lipocytes.

The thickness of these layers varies considerably, depending on the geographic location on the anatomy of the body. The eyelid, for example, has the thinnest layer of the epidermis, measuring less than 0.1 mm, whereas the palms and soles of the feet have the thickest epidermal layer, measuring approximately 1.5 mm.

The dermis is thickest on the back, where it is 30-40 times as thick as the overlying epidermis (James, Berger, & Elton, 2006). The skin organ of regulation the skin aspect of physiology including body temperature view sweat and hair and changes in peripheral circulation of fluid balance view sweat it also act as deserve it for synthesis of vit D.

The skin is an organ of sensation. The skin contains an extensive network of nerve cell that defect and relay the change in environment. There are separate receptors for heat cold touch and pain. Damage to this nerve cell is known as neuropathy, which results in loss of sensation in affected area. The skin is an ultimate vessel for the human body, it receives and transport, accept and expels according to the body needs. It is a container, defender, regulator, breather, feeler and adaptor but success in these roles is not accomplished automatically the skin requires attention and maintenance to function properly. Without such care, the complex organization of skin breaks down.[1]

Skin has three layers;

1. The epidermis, the outermost layer of skin, provides waterproof barriers and creates our skin tone.
2. The dermis, beneath the epidermis, contains tough connective tissue, hair follicles and sweat glands.
3. The deeper subcutaneous tissue (hypodermis) is made of fact and connective tissue. Extremes of temperatures, damaging sunlight and harmful chemical. It also exudes anti-microbial substance that prevents infection and manufacturing vitamin D

for converting calcium into healthy bones.
4. Skin additionally is a huge sensor package with nervous for keeping the brain in touch with the outside world.

1.1.1 EPIDERMIS

The epidermis is a stratified, squamous epithelium layer that is composed primarily of two types of cells: keratinocytes and dendritic cells. The keratinocytes differ from the "clear" dendritic cells by possessing intercellular bridges and ample amounts of stainable cytoplasm (Murphy, 1997). The epidermis harbours a number of other cell populations, such as melanocytes, Langerhans cells, and Merkel cells, but the keratinocyte cell type comprises the majority of the cells by far. The epidermis commonly is divided into four layers according to keratinocyte morphology and position as they differentiate into horny cells, including the basal cell layer (stratum germinativum), the squamous cell layer (stratum spinosum), the granular cell layer (stratum granulosum), and the cornified or horny cell.

Epidermis has four types of cells: -
1. Keratinocytes (skin cells)
2. Melanocytes (pigment produce cells)
3. Langerhans cells (immune cells)
4. Markel cells is a fourth less visible epidermal

1. KERATINOCYTES CELLS

which are characterized by numerous intercellular junctions. The Keratinocytes become more mature or differentiated and accumulate Keratin as they move upward.

The epidermis consists of four distinct layers-

a) Stratum Corneum- Surface, Outside of the Skin

Hardened, flattened dead cells that overlap and create a tough, waterproof protection. Cells are constantly being shed- Desquamation Cell membrane is not visible. It is the uppermost layers and is composed of keratinized cells. The thin membrane consisting of dead nucleus, keratinized cell embedded in a lipid matrix.

b) Stratum Lucidum- Clear Cell

Denucleated cells but not completely hard. Mostly easily visible under a microscope (only on palm and soles. Cell membrane becoming less visible. If present, is a thin, clear layer of dead skin cells in the epidermis; usually seen in thick skin only.

c) Stratum Granulosum-Granular Layer

Cells have a distinct nucleus but cells membranes are dying. Contain granules which are visible in healing tissue after trauma. It is suitable below stratum lucidum and contain of thin layer with 25 layers of flattened rhomboid cells.

d) Stratum Spinosum-Prickle Cell Layer

The stratum spinosum is also known as prickle cell layer and is found on top to the basal layer and together. These two layers are termed the Malpighian layer. Cells are living and membrane is intact, they have fibrils which interlock. > Capable of mitosis (cell division/reproduction) under friction on pressure Le on Soles of feet or palms of hands.

e) Stratum Germinative-Basal Layer

The primary site of cell division/ reproduction (mitosis) in the skin. Cells are living. It is in this layer that cells are made they take about 28-30 days to move up from here through the five layers of the epidermis before being shed.[2]

1.1.2 DERMIS

It is divided into two layers, the superficial area adjacent to the epidermis called papillary region and a deep thicker area known as the reticular dermis. The dermis is tightly connected to the epidermis through a basement membrane. Structural components of the dermis are collagen, elastic fibres, and extrafibrillar matrix. It also contains mechanoreceptors that provide the sense.

Of heat of touch and thermoreceptors. In addition, hair follicles, sweat glands, sebaceous glands (oil glands), apocrine glands, lymphatic vessels, nerves and blood vessels are present in the dermis. Those blood vessels provide nourishment and waste removal for both dermal and epidermal cells.

Layers of the dermis
a) Papilla layer
b) Reticular layer

a. Papilla layer

The papillary dermis is the uppermost layer of the dermis. It intertwines with the rete ridges of the epidermis and is composed of fine and loosely arranged collagen fibres. The papillary region is composed of loose areolar connective tissue. It is named for its finger like projections called papillae or dermal papillae specifically, that extend toward the epidermis and contain either terminal networks of blood capillaries or tactile Meissner's corpuscles.

b. Reticular layer

The lower reticular layer is thicker and made up of thick collagen fibres that are arranged parallel to the surface of the skin. The reticular dermis is the lower layer of the dermis, found under the papillary dermis, composed of dense irregular connective tissue featuring densely-packed.[1,2]

1.1.3 Glands of skin

The skin content two types of glands
a. Sebaceous Glands
b. Sweat gland

a. Sebaceous Glands

Sebaceous glands are found in greatest number on the face and scalp but are present on nearly all other locations of the body with the exception of the tarsal

plate of the eyelids, the buccal mucosa and vermilion borders of the lip, the prepuce and mucosa lateral to the penile frenulum, the labia minora, and the female areola (James et al., 2006). Cells of the sebaceous glands contain abundant lipid droplets known as sebum in their cytoplasm and are arranged into lobules off the upper segment of the hair follicle. Basaloid germinative cells surrounding the lobule give rise to the lipid- filled cells, which are then expelled into the infundibular segment of the hair follicle via the sebaceous duct. The sebaceous glands are thought to be evolutionarily important contact with the birth canal including the vertex, anterior scalp over the forehead and nose to the lower jaw line, and the shoulders, chest, and upper aspect of arms posteriorly. Eccrine sweat glands are involved in the regulation of heat and are most abundant on the soles of the feet and least plentiful on the back (Murphy, 1997 Sato & Dobson, 1970). The sweat glands originate as a band of epithelial cells growing downward from the epidermal ridge (Mauro & Goldsmith, 2008). This tubular, or ducktail, structure is modified during development to generate.

b. Sweat gland

The composite parts of the eccrine sweat unit, which are the intraepidermal spiral duct, the straight dermal portion, and the coiled secretary duct (James et al., 2006; Mauro & Goldsmith). Apocrine Sweat Glands whereas eccrine glands are primarily involved in thermal regulation, apocrine glands are involved in scent release (Murphy, 1997). Apocrine sweat glands in humans are confined mainly to the regions of the axillae and perineum, and unlike eccrine and apocrine glands, they do not open directly to the skin surface. The skin has very important vital functions for keeping the physiological and biochemical condition of the body in its optimum state.[3]

The most important functions of the skin are:

1. Provides a protective barrier against mechanical, thermal and physical injury and noxious agents.
2. Prevents loss of moisture.
3. Reduces the harmful effects
4. Acts as a sensory organ of UV radiation.
5. Helps regulate temperature control.
6. Has a cosmetic, social and sexual association.
7. Exercise toxic substance with sweat.[1]

A transdermal film was developed in 1970s and FDA approved it in 1979s for motion sickness treatments, a transdermal film which is also called a skin film is a medicated adhesive dosage form placed on skin and act as delivery for a specific dose of drug to be provided through the skin and into blood body circulation. [4] Anew efforts for drug delivery are by using the skin as an application site to deliver the drug into body blood stream at predetermined rate and maintains the drug blood concentration within therapeutic range. Transdermal drug first-pass metabolism, minimized systemic toxicity incidence and patient compliance improvement. For typical transdermal administration, the drug should have many physiochemical properties such as short half-life, small dose and low molecular weight.[5]

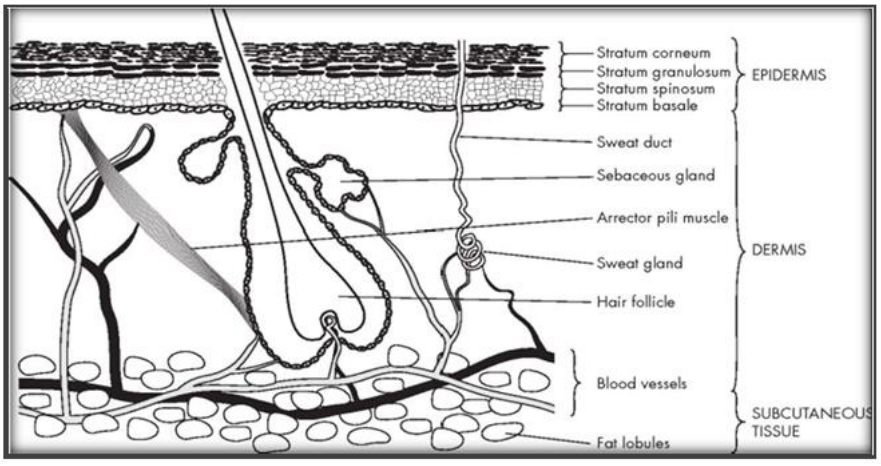


Fig No. 1: - Diagram of Skin.

The most common form of drug delivery is the oral route. In this route of administration has notable advantages and also has significant drawbacks such as first-pass metabolism, drug degradation in gastrointestinal tract due to enzymes, and PH. To overcome these difficulties a novel drug delivery system was developed.[6] Transdermal drug delivery systems (TDDS), also known as "patches," are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin.[7] Transdermal delivery not only provides controlled, constant administration of the drug, but also allows continuous input of drugs with short biological half- lives and eliminates pulsed entry into systemic circulation. Transdermal patch uses a special membrane to control the release rate at which the liquid drug contained patch reservoir can pass through the skin and into the bloodstream.[8] Several important advantages of transdermal drug delivery are limitation of hepatic first-pass metabolism, enhancement of therapeutic efficiency, and maintenance of steady

plasma level of the drug.[8]

Advantages

- Transdermal medication delivers a steady infusion of the drug over prolonged period of time, therefore, avoiding adverse side effects and therapeutic failure frequently associated with intermittent dosing can also be avoided.
- Alternative route of administration for the patients who cannot tolerate oral dosage
- Avoidance of first pass metabolism because it bypasses the liver.
- Self-administration is possible, and they are non-invasive, avoiding the inconvenience of parenteral therapy.
- They are easily and rapidly identified in emergencies (for example, unresponsive, unconscious, or comatose patient) because of their physical presence, features, and identifying markings.[9]
- The mechanism of action used by these systems involves perturbing the stratum corneum, contravening the tight junctions, and disturbing the cell membrane structure, thereby expediting drug penetration
- The transdermal route has drawn considerable attention and has emerged as a solid alternative to mimic the drawbacks of drug delivery through the oral and parenteral routes. However, the effectiveness of TDDS is often limited by the skin's outermost layer, the stratum corneum (SC), which acts as a barrier to drug diffusion.
- Minimal inter and intra patient variation because the composition of skin structurally and biologically is the same in almost all the humans.
- Steady and optimum blood concentration time profile achieved which reduce adverse effects
- Release of drug for prolonged time with single application which extend the duration of activity.
- Drugs entity with short biological half-lives and narrow therapeutic window are utilized.
- Avoiding the fluctuation in plasma level of drug.
- Termination of therapy is easy at any point of time.
- When oral route is unsuitable as with vomiting and diarrhea then transdermal route is used as alternate for deliver the drug candidate

Disadvantages

Although transdermal drug delivery systems possess numerous advantages, these also have some disadvantages as follow:

- Difficult to administer the large dose, i.e., more than 10 mg/day.
- Ionic drugs create problems
- Drugs having size more than 500 Dalton are not suitable for TDDS.
- Drugs in high concentration may cause skin irritation.
- Difficult to achieve high plasma drug concentration.
- Long-term adherence creates discomfort to patients.
- Current transdermal drug delivery technologies, like patches and ointments, effectively
- deliver low molecular weight drugs through the skin. However, delivering larger, hydrophilic drugs and macromolecules remains a challenge. In the present study,
- Topical or transdermal drug delivery behaves as a challenging system because the skin acts as a natural and protective barrier
- The delivery system is not suitable for drugs that require high blood levels
- Skin irritation may occur in some patients at the site of application
- This system is uneconomical
- Dose dumping may occur due to Binding of drug to skin
- Therapeutic performance of the system affected by Cutaneous metabolism
- It can be used only for chronic conditions not for acute condition because chronic condition require drug therapy for a long period of time e.g., hypertension, angina and diabetes etc.
- Drugs with very low or high partition coefficient fail to reach systemic circulation.[10] Diclofenac is non-steroidal anti-inflammatory agent, widely used to reduce the pain and inflammation in arthritis, toothache, Trauma, Wound, burn etc. Transdermal films of Diclofenac Sodium were formulated by using different polymer combinations such as hydrophilic - lipophilic polymers (Methyl cellulose: Poly vinyl alcohol).

The medicated films were evaluated for physicochemical properties and also medicated films were evaluated for area variation, drug content and percent cumulative drug release. In vitro drug release study. Primary irritation study shows that the transdermal films are non-irritant. Transdermal patches offer added advantages such as maintenance of constant and prolonged drug level, reduced frequency of dosing, self-administration and easy termination of medication leading to patient compliance.[11]

Solution to Problem

The present inventors have found that a patch in which an adhesive layer contains an adhesive base and diclofenac sodium and the content of diclofenac sodium is 1.50 to 2 mg per cm^2 of application area is effective in relieving headache.

A patch of the present invention is a patch for relieving headache, the adhesive patch comprising a backing and an adhesive layer laminated on the backing, wherein the adhesive layer contains an adhesive base and 1.50 to 2 mg of diclofenac sodium per cm^2 of application area, and the patch is used by applying the patch once a day.[12]

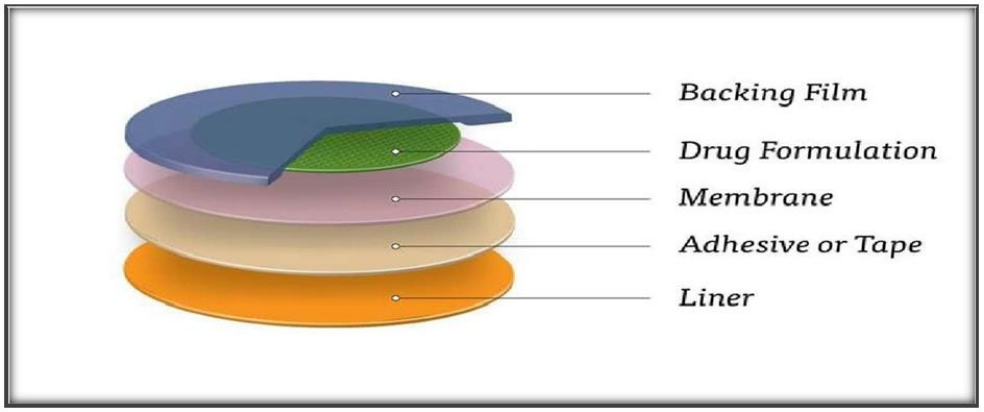


Fig. No. 2: - Structure of Patch.

Transdermal Patch and its Components

1. Backing membrane

Backing membranes are flexible and they provide a good bond to the drug reservoir, prevent drug from leaving the dosage form through the top, and accept printing. It is impermeable substance that protects the product during use on the skin e.g. metallic plastic laminate, plastic backing with absorbent pad and occlusive base plate (aluminum foil), adhesive foam pad (flexible polyurethane) with occlusive base plate (aluminum foil disc) etc.

- **Purpose**

The backing membrane is the outermost layer of a transdermal patch, providing a barrier against the external environment.

- **Function**

It protects the drug formulation, offers structural support, and often carries printed product information.

Materials

Common materials include polyolefins, polyesters, and elastomers, often in clear, pigmented, or metallized forms.

- **Flexibility**

Backing materials need to be flexible yet possess good tensile strength to conform to body movements and maintain adhesion.

- **Example**

Metallic plastic laminates, plastic backing with an absorbent pad, or adhesive foam pads with an occlusive base plate.

- **Buccal Tablets**

The backing membrane serves a similar purpose, providing a protective layer and structural support for the drug formulation.

- **Membrane Filtration**

In filtration systems, a backing layer (like Membrane) can improve adhesion, prevent bleed-through, and reduce defects in the membrane.

In essence, the backing membrane acts as a shield, providing a stable platform for drug delivery and protecting the formulation during its application and use.

2. Drug reservoir/Matrix

The layer on a transdermal patch that provides structure and protects the drug This method involves uniformly dispersing drug particles in a hydrophilic (or lipophilic) polymer **matrix** to create the **drug reservoir**. A disc with a specific surface area and controlled thickness is then formed from the resulting polymer **matrix**.

Unlike the Single layer and Multilayer Drug in adhesive systems the reservoir transdermal system has a separate drug layer. The drug layer is a liquid compartment containing a drug solution or suspension separated by the adhesive layer. This patch is also backed by the backing.

The Matrix system has a drug layer of a semisolid matrix containing a drug solution or suspension. The adhesive layer in this patch surrounds the drug layer partially overlaying it.

Contains the drug either in a reservoir (gel/liquid) or matrix (solid/semi-solid) form.

Polymer Matrix

Essential Characteristics for Polymers in Transdermal Delivery Systems

- The polymer's molecular weight and chemical properties must facilitate the effective diffusion and controlled release of the specific drug.
- It should remain chemically stable and inert, ensuring no adverse reactions with the drug.
- The material must be safe, exhibiting no toxicity or negative interactions with the patient.
- Should be straightforward to produce and shape into the required form.
- Cost-effectiveness is important for practical manufacturing.
- Capable of incorporating substantial quantities

of the active pharmaceutical ingredient.

3. Rate-Controlling Membrane

Controls the rate at which the drug diffuses from the patch to the skin**.** The rate-controlling membrane in transdermal patches regulates the release of the drug from the reservoir or multilayer patches. Key characteristics of this membrane include: Regulated drug release: Controls the rate at which the drug is released. Flexibility: Should be flexible enough to withstand bending or stretching without splitting or cracking. Material options: Common materials used for rate-controlling membranes include

a. Polyethylene sheets
b. Cellulose acetate
c. Ethylene vinyl acetate co-polymer.[27]

4. Adhesive Layer

For both **classes** of TDDS, pressure-sensitive adhesives (PSAs) play a major role, serving as the matrix that carries everything active (such as additives and permeation enhancers) and the means for making the patch stick to the skin. There are three major families of PSAs: rubber-based PSAs, acrylic PSAs in the form of acrylic solutions, emulsion polymers or hot melts, and silicon PSAs. For each family of adhesives there are several sub-categories that give the required flexibility to the formulator.

Each active is different and the choice of adhesives is critical for the success of the final product. PSA adheres patches to skin without residue. Examples: polyacrylates, polyisobutylene, silicone.

Selection depends on patch design and drug. PSA must be safe and not alter drug release.

. Both adhesive systems should fulfill the following criteria:

- Should adhere to the skin aggressively, should be easily removed.
- Should not leave an unwastable residue on the skin.
- Should not irritate or sensitize the skin. The face adhesive system should also fulfill the following criteria.
- Physical and chemical compatibility with the drug, excipients and enhancers of the device of which it is a part.
- Permeation of drug should not be affected.
- The delivery of simple or blended permeation enhancers should not be affected.

Acrylics

1. With or without functional groups
2. Cross-linked or not Solutions, hot melts or emulsions

Silicon-Based Adhesives

1. Standard
2. Amine-compatible

5. Release Liner

A peelable protective layer removed before applying the patch. Generally, a release liner is a film covered with an anti-adherent coating. The role of the release liner is to protect the system as long as it is in the package, and it is removed just before the adhesion of the TDDS to the skin. Release liners play a crucial role in the stability of the product and in its safe and functional use. The release liner must therefore be chosen very carefully. An incorrect release liner does not permit the easy release of the patch, and can interfere with the active(s) or other components, thereby reducing its shelf life. The most common films used as release liners are paper-based, plastic film-based and composite films. The two major classes of coating are silicones and fluoro-polymers.

Typically, there are two formats of release liners: single-side coated and double-side coated liners provide protection for an adhesive that is laminated to a film or paper substrate. These liners primarily serve as a delivery mechanism for adhesives undergoing automatic or manual applications. Double sided liners, also referred to as differential release liners, are coated on both sides with release coatings designed to provide differing release values Release liners can come in many different materials, paper, poly-coated paper, polyester film, polyethylene, or polypropylene, and may be coated on one side to provide a non-stick surface. They are used in numerous applications in conjunction with various pressure-sensitive tapes and converted solutions. The released coatings can be either silicone or non-silicone.

Types of Transdermal Patches Single-layer Drug-in-Adhesive

The Single-layer Drug-in-Adhesive system is characterized by the inclusion of the drug directly within the skin contacting adhesive. In this transdermal system design, the adhesive not only serves to affix the system to the skin, but also serves as the formulation foundation, containing the drug and all the excipients under a single backing film. The rate of release of drug from this type of system is dependent on the diffusion across the skin.

Multi-layer Drug-in-Adhesive

The Multi-layer Drug-in-Adhesive is similar to the Single-layer Drug-in-Adhesive in that the drug is incorporated directly into the adhesive. However, the multi-layer encompasses either the addition of a membrane between two distinct drug-in adhesive layers or the addition of multiple drug-in-adhesive layers under a single backing film.

Drug Reservoir-in-Adhesive

The Reservoir transdermal system design is characterized by the inclusion of a liquid compartment containing a drug solution or suspension separated from the release liner by a semi-permeable membrane and adhesive. The adhesive component of the product

responsible for skin adhesion can either be incorporated as a continuous layer between the membrane and the release liner or in a concentric configuration around the membrane.

Drug Matrix-in-Adhesive

The Matrix system design is characterized by the inclusion of a semisolid matrix containing a drug solution or suspension which is in direct contact with the release liner. The component responsible for skin adhesion is incorporated in an overlay and forms a concentric configuration around the semisolid matrix.

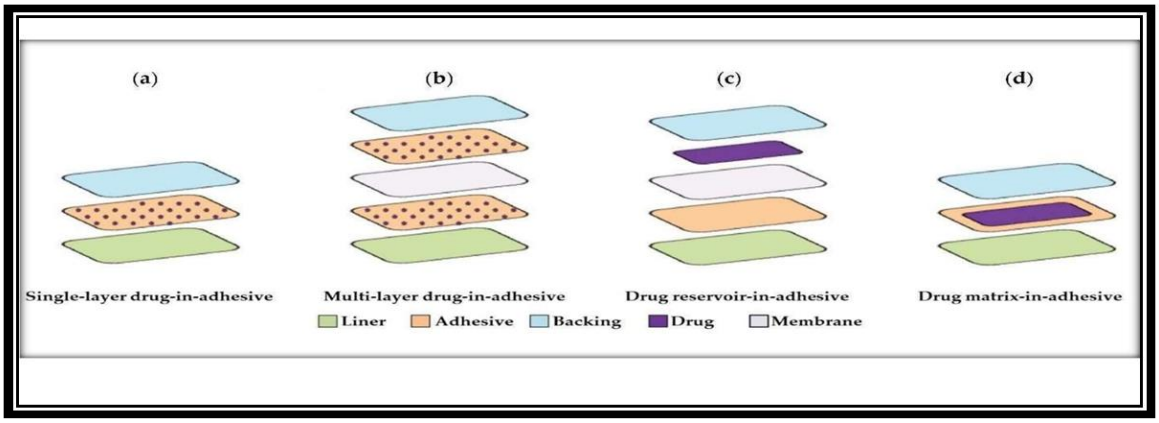


Fig. No. 3: - Structure of Types of Transdermal Patches.

LITERATURE SURVEY

1. Niharika, Navneet Verma et.al (2016)

In this review article, Adhesive Polymers in Fabrication of Transdermal Drug delivery, covers a brief outline of various method involved in the preparation of transdermal patches, various adhesives being used commercially, assortment of adhesion parameters, and utilization of adhesion criterion, advancement and application of adhesive technology in transdermal therapy. The article also provides groundwork of recent development of adhesive based technology in transdermal along with the future aspects.[13]

2. Suksaeree, Patsakorn Siripornpinyo, and Somruethai Chaiprasit et.al (2017)

In this research article, Characterization, and In Vitro Evaluation of Transdermal Patches for Inhibiting Crystallization of Mefenamic Acid Jirapornchai. covers crystallization of mefenamic acid in transdermal patch is a major problem that makes the patch unstable and decreases the drug release. The additive was used to inhibit crystallization of a mefenamic acid. Among the different types of additives, polyvinylpyrrolidone (PVP) K30 and PVP K90 were studied and found to be highly effective in inhibiting the crystallization of the drug.[14]

3. Jagtap S.B. et.al (2017)

In this International Journal of Chem. Tech Research Formulation and Evaluation of Transdermal Patch of Iodine as Ladies Bindi, Sawant D.A.2 given that Iodine is more important in pregnant women and need of iodine is also more in pregnancy Hence, I attempt was made to prepare and evaluate A transdermal patch containing iodine for ladies as a model drug by solvent casting method using hydrophilic, and lipophilic polymers.[15]

4. Raja Rajeswari Kamisetti et.al (2017)

International Journal of Research in Pharmacology & Pharmacotherapeutics Fight the iodine deficiency: advances in the iodine supplement as lifesaving dot-- a critical review on Iodine deficiency is a global health issue and Chronic, severe iodine deficiency in utero causes cretinism, a condition characterized by mental retardation.[16]

5. Sudarshan Jagtap1, Pallavi Badhe2, Dr.p Gujarathi1, lll et.al(2018)

Formulation and Evaluation of Transdermal Patch of Diclofenac Sodium as Ladies Bindi for Treatment of Rheumatoid Arthritis, traditionally physicians prescribed Diclofenac tablet for the treatment of Rheumatoid Arthritis in geriatrics patients, the survey of Rheumatoid Arthritis states that the disease is common in females than in males. Diclofenac sodium used for topical applications and can be absorbed transdermal. Rather than the Transdermal patch we are formulated a TDDS as ladies bindi to enhance the Patient compliance.[11]

6. Zainab E. Jassim et.al (2018)

Transdermal drug delivery system: A review told that Transdermal drug delivery has made an important contribution to medical practice but has yet to fully achieve its potential as an alternative to oral delivery and hypodermic injections. The transdermal drug delivery systems (TDDS) review articles provide information regarding the transdermal drug delivery systems and its evaluation process as a ready reference for the research scientist who is involved in TDDS.[17]

7. **Zainab Ahmed Sadeq, Nawal A. Rajab, Shaimaa Nazar Abd Alhammid, Hiba Zaki et.al (2019)**

Preparation, in-vitro Evaluation, Mechanical Characterization, and Release Of Nebivelol Hydrochloride as A Transdermal Film using combined Eudragite-Polyvinyl Alcoholas Adhesive Film Forming Polymer The main objective of this study was to prepare Nebivelol Hydrochloride (NEB) as transdermal film using combined Eudragit E and PVA as adhesive film forming polymer.

8. **M. R. Shivalingam, arul balasubramanian, kothai ramalingam et.al (2021)**

Formulation and evaluation of transdermal patches of pantoprazole sodium. This present study was an attempt to develop an alternative dosage form for the existing conventional oral, parenteral proton pump. Inhibitor (ppi) as transdermal patches for treating peptic ulcers.[19]

9. **Y.Krishna Reddy, D. Maheswara Reddy, M.Asok Kumar et.al (2021)**

Drug delivery through the skin to achieve a systemic effect of a drug is commonly known as transdermal drug delivery and differs from traditional topical drug delivery. Transdermal drug delivery system (TDDS) is the system in which the delivery of the active ingredients.

10. **Sudarshan Jagtap1, Pallavi Badhe2, Dr.p Gujarathi1, lll et.al(2018)**

Formulation and Evaluation of Transdermal Patch of Diclofenac Sodium as Ladies Bindi for Treatment of Rheumatoid Arthritis, traditionally physicians prescribed Diclofenac tablet for the treatment of Rheumatoid Arthritis in geriatrics patients, the survey of Rheumatoid Arthritis states that the disease is common in females than in males. Diclofenac sodium used for topical applications and can be absorbed transdermal. Rather than the Transdermal patch we are formulated a TDDS as ladies bindi to enhance the Patient compliance.[11]

11. **Raja Navamanisubramanian1, Raghunandan Nerella1, Chamundeeswari D3, Shanmuganathan Seetharaman, lll et.al(2017)**

Transmucosal buccal drug delivery could be an alternative for oral administration for systemic delivery of Verapamil Hydrochloride (VH), as it has low bioavailability 20 - 35 % due to its extensive first pass metabolism and variable absorption at GIT.

12. **Patricia M Kearney, Colin Baigent, Jon Godwin, Heather Halls, Jonathan R Emberson, Carlo Patrono et.al (2005)**

To assess the effects of selective cyclo-oxygenase-2 (COX 2) inhibitors and traditional non-steroidal anti-inflammatory drugs (NSAIDs) on the risk of vascular events.

13. **Patricia M Kearney, Colin Baigent, Jon Godwin, Heather Halls, Jonathan R Emberson, Carlo Patrono et.al(2006)**

To assess the effects of selective cyclo-oxygenase-2 (COX 2) inhibitors and traditional non- steroidal anti-inflammatory drugs (NSAIDs) on the risk of vascular events. Selective COX 2 inhibitors are associated with a moderate increase in the risk of vascular events, as are high dose regimens of ibuprofen and diclofenac, but high dose naproxen is not associated with such an excess.

14. **Varsha J. Galani et.al(2019)**

Musa paradisiaca Linn. is a popular Indian medicinal plant belonging to the Musaceae family. This plant commonly known as plantain or banana is highly eating nutritious fruit over the world. A wide range of phytochemical constituents have been isolated from this plant. It has long been used in traditional Ayurvedic Indian medicine for various diseases. This plant is pharmacologically studied for analgesic activity, antidepressant activity, adaptogenic activity, anticonvulsant activity, CNS depressant activity, antidiarrheal activity, antiurolithiatic activity, antiulcerative activity, antimicrobial activity, antidiabetic activity, antioxidant activity, antilipidemic activity, antihypertensive activity, antiatherosclerotic activity, cytotoxic activity, Thrombolytic activity, Antimalarial activity, Antisnakevenom activity, Mutagenic activity, Hepatoprotective activity, Hair growth promoting activity, Wound healing activity, Bioabsorptive activity and Tablet disintegrant activity and many other activities. A comprehensive account of the morphology, phytochemical constituents, traditional uses, and pharmacological activities reported are included in view of the many recent findings of importance on this plant.

15. **Vijai Lakshmi*, Santosh Kumar Agarwal, Abbas Ali Mahdi et.al(2015)**

As the people are becoming aware of the potency and side effect of syn thetic drugs, there is an increasing interest in the natural product rem edies with a basic approach towards the nature all over the world. Many infectious diseases have been treated with herbals throughout the history of mankind. Medicinal plants play a vital role for the development of new drugs. It is estimated that about eighty percent of the world s population residing in the vast rural areas of the developing and under developed countries, still rely mainly on medicinal plants. Medicinal plants are the only affordable and accessible source of primary health care for them, especially in the absence of access to modern medical facilities. In this review literature on of Musa paradisiaca Linn. pharmacological activities as well as the chemical constituents have been summarized.

AIM

Formulation and In-Vitro Evaluation of Medicated Patch Containing Natural Release Retardant.

OBJECTIVES

- To formulate a painless method of delivering drugs systemically by applying a drug formulation onto intact and healthy skin.
- To study the medicated patch as an alternative route of administration.
- To incorporate a natural binder in a transdermal patch.
- To incorporate a natural release retardant in a transdermal patch.
- To evaluate the medicated Patch.

RATIONALE

- It provides a specific, predetermined dose of medication that is absorbed through the skin and into the bloodstream.
- Patches offer smooth, continuous delivery of drug through the skin into the bloodstream.
- This avoids passage through the gastrointestinal tract, therefore independent of food intake. Transdermal delivery also avoids the first-pass effect.
- 'patch' to enhance the Patient compliance and patient does not feel like that she was taking a medicine by application
- Transdermal patches offer a non-invasive and painless method of drug delivery, with the added benefit of providing a consistent therapeutic dosage over a predetermined time period.
- That its utility is maximized through reduction in side effects and care and control of headache condition in shortest possible time by using smallest quantity of drug administered by TDDS.
- The immediate release drug delivery system lack's some feature's like dose maintenance and control release rate and site targeting.

PLAN OF WORK

The aim of the present study was to develop different transdermal matrix films with varied ratios of hydrophilic and lipophilic combination containing the drug Diclofenac sodium and to perform the physicochemical and in vitro evaluation along with primary irritation study of the prepared films. The purpose was to provide the delivery of drug at a controlled rate across intact skin to achieve a therapeutically effective drug level for a longer duration of time from transdermal patch.

This is a plan of work for accomplishing above objectives: -

- Introduction
- Literature survey
- Procurement of chemicals and drug
- Polymer-Drug compatibility study
- Natural Release retardant study
- Formulation of Transdermal patch
- Transition of formulated patch
- *In vitro* Evaluation of medicated
- Result and Discussion
- Summary and Conclusion
- References

Table no. 1: Name of Ingredient, Category and Manufacturer.

Sr. No	Name of Ingredient	Category	Manufacturer
1	Diclofenac sodium	API	Pallav
2	Polyvinyl alcohol (PVA)	Polymer	Pallav
3	Methyl cellulose (MC)	Polymer	Pallav
4	Propylene glycol (PG)	Plasticizer	Pallav
5	Methanol	Solvent	Loba chemie Pvt.
6	Glycerol	Plasticizer	Pallav
7	Banana peel extract	Release retardant (Binder)	-
8	Okra extract	Release retardant (Binder)	-
9	DMSO	penetration enhancer	Pallav
10	Backing membrane	Backing membrane	-

ACTIVE PHARMACEUTICAL INGREDIENTS

1. DICLOFENAC SODIUM

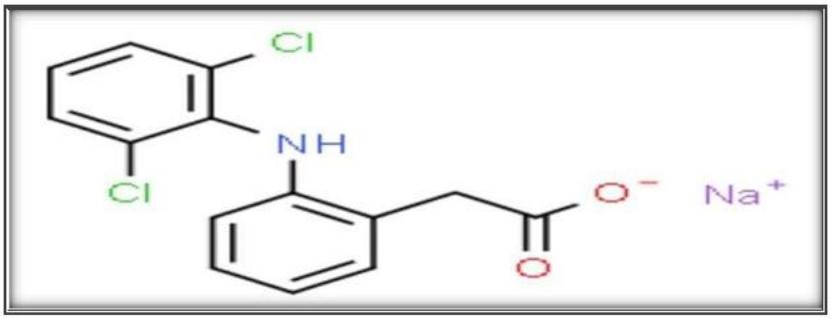


Fig. No.4: - Structure of Diclofenac Sodium IUPAC name: - [2-(2, 6-Dichloroanilino) phenyl] acetic acid
pH Value: - 8.15

Molecular Weight: - 318.13
Solubility: - sparingly soluble in water, freely soluble in methanol (organic solvent).[20]

DOSE FOR DIFFERENT FORMULATIONS

Diclofenac sodium is a non-steroidal anti-inflammatory agent widely used to reduce the pain & inflammation in arthritis, Toothache, Trauma, Wound, burn, etc. It works by blocking your body's production of certain natural substances that cause inflammation. This effect helps to decrease swelling, pain, or fever.

Diclofenac, sold under the brand name Voltaren among others, is a nonsteroidal anti-inflammatory drug (NSAID) used to treat pain and inflammatory diseases such as gout.[5][8] It can be taken orally (swallowed by mouth), inserted rectally as a suppository, injected intramuscularly, injected intravenously, applied topically to the skin, or through eye drops.[8][11][12] Improvements in pain last up to eight hours.[8] It is also available as the fixed-dose combination diclofenac/misoprostol (Arthrotec) to help protect the stomach; however, proton pump inhibitors such as omeprazole are typically first-line since they are at least as effective as misoprostol, but with better tolerability.

Common side effects include abdominal pain, gastrointestinal bleeding, nausea, dizziness, headache, and swelling.[8] Serious side effects may include heart disease, stroke, kidney problems, and stomach ulceration.[14][8] Use is not recommended in the third trimester of pregnancy.[8] It is likely safe during breastfeeding.[14] Diclofenac is believed to work by decreasing the production of prostaglandins, like other drugs in this class.[16]

In many countries, eye drops are sold to treat acute and chronic nonbacterial inflammation of the anterior part of the eyes (such as postoperative states).[22] The eye drops have also been used to manage pain for traumatic corneal abrasion.

Diclofenac is also available in topical forms and is useful for osteoarthritis but not other types of long-term musculoskeletal pain.[20] Diclofenac may also help with actinic keratosis and with acute pain caused by minor strains, sprains and contusions.[21]

➢ **Tablets (25 mg and 50 mg)**

Therapeutic Goods Administration Inflammatory and degenerative forms of rheumatism: rheumatoid arthritis and osteoarthritis. Relief of acute or chronic pain states in which there is an inflammatory component. Symptomatic treatment of primary dysmenorrhea.

Suppositories (12.5 mg, 25 mg, 50 mg or 100 mg)

Inflammatory and degenerative forms of rheumatism: rheumatoid arthritis and osteoarthritis. Short term (up to three days) treatment of post-operative pain in children.

➢ **Diclofenac rapid release (50 mg)**

As short-term treatment (up to one week) for the relief of acute pain states in which there is an inflammatory component. Treatment of acute migraine attacks (with or without aura). Symptomatic treatment of primary dysmenorrhea.

3% diclofenac gel

Management of actinic keratoses.

There are several OTC products (S3, S2 and unscheduled), the indications are as follows:

➢ **Diclofenac rapid release (25 mg) tablet (S3)**

As short-term treatment (up to one week) for the relief of acute pain states in which there is an inflammatory component. Treatment of acute migraine attacks (with or without aura). Symptomatic treatment of primary dysmenorrhea.

➢ **Diclofenac rapid release (12.5 mg) tablet (S2)**

Relief of headache, dental pain, period pain, rheumatic and muscular pain, backache. Relief of symptoms of colds and flu, including aches and pains, sore throat pain. Reduction of fever. Dermal products containing $1% diclofenac (unscheduled)

For the short term (up to 2 weeks) local symptomatic treatment of the following musculoskeletal inflammatory conditions. Acute soft tissue injuries, including sprains, strains, tendinitis and sports injuries. Localized forms of soft tissue rheumatism, e.g., tendinitis (tennis elbow) and bursitis. For the short term (up to 3 weeks) relief of pain in non-serious arthritis (i.e. mild and localised forms of osteoarthritis) of the knee or fingers. Relief of osteoarthritic pain.

➢ **MECHANISM OF ACTION**

Diclofenac has analgesic, anti-inflammatory, and antipyretic properties. It causes inhibition of cyclooxygenase (COX-1 and COX-2) and act as a potent inhibitor of prostaglandin synthesis in vitro.

➢ **USES**

a. Diclofenac is a medicine that reduces swelling (inflammation) and pain. It's used to treat aches and pains, as well as problems with joints, muscles and bones**.**

b. Diclofenac is used to treat mild to moderate pain. It is prescribed for joint pain, inflammation.

c. Transdermal diclofenac is used to treat short-term pain due to minor strains, sprains, and bruises in adults and children 6 years of age and older. Diclofenac is in a class of medications called nonsteroidal anti-inflammatory drug.

d. Diclofenac reduces joint stiffness from arthritis.

➢ **SIDE EFFECTS**

1. Upset Stomach,

2. Nausea,
3. Heartburn,
4. Diarrhea,
5. Constipation,
6. Headache,
7. Drowsiness,
8. Blurred Vision May Occur,
9. Dizziness.

2. POLYVINYL ALCOHOL

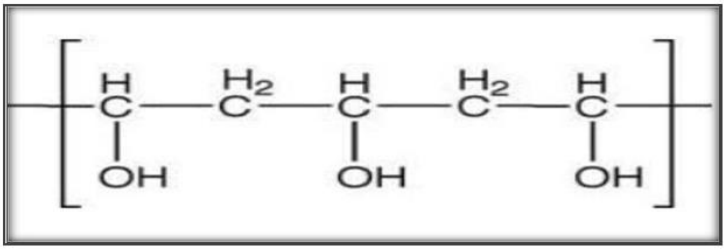


Fig. No.5: - Structure of Polyvinyl Alcohol.

IUPAC name: - butan-2-ol
Melting Point: - 180-190 ^{0}C
Boiling Point: - 228 ^{0}C
pH value: - 5.0 - 6.5
It has a molecular weight of between 26,300 and 30,000 A degree of hydrolysis of 86.5 to 89%.
Nature: - Crystalline

Properties

- PVA is partially crystalline upon formation and is characterized by properties such as chemical resistance, water solubility, and biodegradability. The similarity in physical properties makes it compatible with human tissues.
- Polyvinyl alcohol has excellent film-forming, emulsifying, and adhesive properties. It is also resistant to oil, grease, and solvents. It has high tensile strength and flexibility, as well as high oxygen and aroma barrier properties. However, these properties are dependent on humidity: water absorbed at higher humidity levels acts as a plasticizer, which reduces the polymer's tensile strength, but increases its elongation and tear strength.

3. METHYL CELLULOSE

Methyl cellulose (or methylcellulose) is a compound derived from cellulose. It is sold under a variety of trade names and is used as a thickener and emulsifier in various food and cosmetic products, and also as a bulk-forming laxative. Like cellulose, it is not digestible, not toxic, and not an Allergan.

Methyl cellulose (MC) is the most important commercial cellulose ether. It is also the simplest derivative where methoxy groups have replaced the hydroxyl groups. The most important properties of this non-ionic polymer are its water solubility and its gelation when exposed to heat. Although soluble in water, films made from methyl cellulose usually retain their strength and do not become tacky when exposed to humidity. Polymer films made of methyl cellulose have excellent strength (60 – 70 Mpa) and low elongation (5 – 15 %) at room temperature (75°F) but their strength decreases rapidly with increasing temperature. MC also has excellent UV, oil, and solvent resistance.

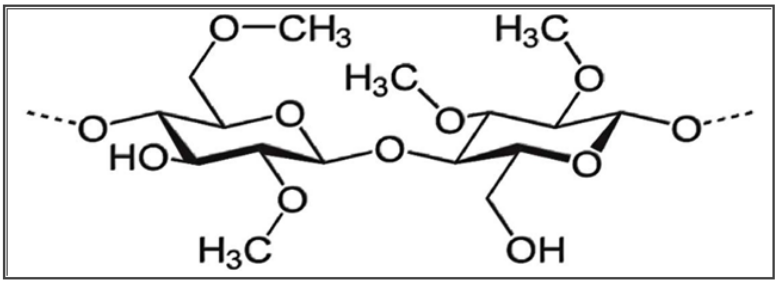


Fig.no.6: - Structure of Methyl Cellulose.

Chemical formula: - $C_{20}H_{38}O_{11}$
IUPAC NAME: - Methyl 2,3,4,6-tetra-O-methyl-hexopyranosyl-(1->4)-2,3,6-tri-methyhexopyranoside
Boiling Point: - 507 ^{0} C **Melting Point: -** 305^0 C **Uses: -**

a. Skim coat / wall putty
b. Tile adhesives
c. Joint fillers
d. Cement mortar/Masonry mortar
e. Cement based plasters
f. External insulation and finish systems (EIFS)
g. Grout
h. Self-Levelling
i. Detergent

4. PROPYLENE GLYCOL

Propylene Glycol is most commonly used co-solvent

surfactant. Moisturize the skin. Di propylene glycol is a mixture of three isometric chemical compounds, 4-oxa-2,6-heptandiol, 2(2-hydroxy- propoxy)-propan-1-ol, and 2-(2-hydroxy-1-methyl-ethoxy)-propan-1-ol. It is a colorless, nearly odourless liquid with a high boiling point and low toxicity.

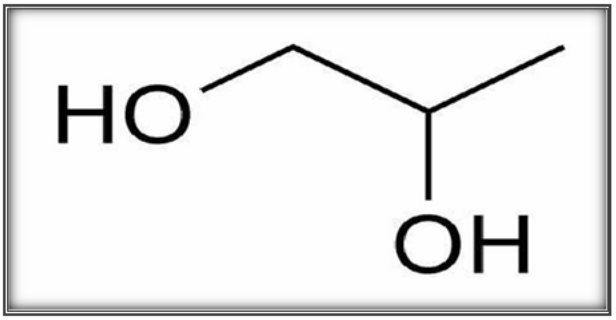


Fig. No. 7: - Structure of Propylene Glycol.

Table No. 2: Properties of Propylene Glycol.

IUPAC NAME	propane-1,2-diol
Chemical Formula	$C_3H_8O_2$
CAS Number	55-57-6
Appearance	Colourless liquid
Odour	Odourless
Boiling Point	188.2^0 C
Solubility	Miscible in water, Ethanol, diethyl ether, acetone, chloroform
Molar mass	76.095 g mol^{-1}
Empirical formula	$C_3H_8O_2$
Description	It is the viscous colourless liquid in which is nearly odourless but possess a faintly sweet taste.
Melting point	-59^0 C

Uses

Propylene glycol finds many uses as a plasticizer, an intermediate in industrial chemical reactions, as a polymerization initiator or monomer, and as a solvent. Its low toxicity and solvent properties make it an ideal additive for perfumes and skin and hair care products. It is also a common ingredient in commercial fog fluid, used in entertainment industry fog machines.[21]

5. METHANOL

Methanol, also known as methyl alcohol, amongst other names a chemical and the simplest alcohol, with the formula CH_3OH (a methyl group linked to a hydroxyl group, often abbreviated MeOH). It is a light, volatile, colourless, flammable liquid with a distinctive alcoholic odour similar to that of ethanol (potable alcohol). A polar solvent methane acquired the name wood alcohol because it was once produced chiefly by the destructive distillation of wood. Today, methanol is mainly produced industrially by hydrogenation of carbon monoxide.

Methanol consists of a methyl group linked to a polar hydroxyl group. With more than 20 million tons produced animally, it is used as a precursor to other commodity chemicals, includingformaldehyde, acetic acid, methyl tart butyl ether, methyl benzoate, anisole, pHenoxyacids, as well as a host of more specialised chemicals.

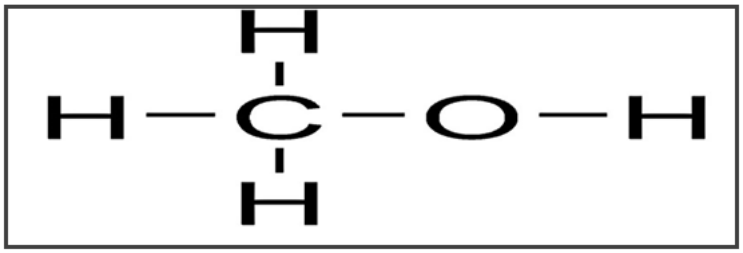


Fig. No. 8: - Structure of Methanol.

Properties

- Chemical formula: - CH_3OH or CH_4O
- Molar mass: -32.04 g mol^{-1}
- Appearance: -Colourless liquid
- Odour: -Sweet and pungent
- Density: - 0.792 g/cm^3

- Melting point: - 97.6°C (-143.7 F; 175.6 K)
- Boiling point: - 64.7 °C (148,5 °F; 337.8K)
- Solubility in water: - miscible
- Vapor pressure: - 13.02 kPa (at 20 °C)

Applications

➢ **Formaldehyde, acetic acid, methyl tert-butyl ether**

Methanol is primarily converted to formaldehyde, which is widely used in many areas, especially polymers. The conversion entails oxidation:
Acetic acid can be produced from methanol.

➢ **Methanol to hydrocarbons, olefins, gasoline**

Condensation of methanol to produce hydrocarbons and even aromatic systems is the basis of several technologies related to gas to liquids. These include methanol-to- hydrocarbons methanol to gasoline (MtG), methanol to olefins (MtO), and methanol to propylene (MtP). These conversions are catalysed by zeolites as heterogeneous catalysts. The MtG process was once commercialized at Montuno in New Zealand.

➢ **Gasoline additive**

The European Fuel Quality Directive allows fuel producers to blend up to 3% methanol, with an equal amount of cosolvent, with gasoline sold in Europe, China uses more than 4.5 billion liters of methanol per year as a transportation fuel in low level blends for conventional vehicles, and high- level blends in vehicles designed for methanol fuels).

Production

Carbon monoxide and hydrogen react over a catalyst to produce methanol. Today, the most widely used catalyst is a mixture of copper and zinc oxides, supported on alumina, as first used by ICI in 1966. At 5-10 MPa (50-100 ATM) and 250°C (482 °F), the reaction is characterized by high selectivity (>99.8%). The production of synthesis gas from methane produces three moles of hydrogen for every mole of carbon monoxide, whereas the synthesis consumes only two moles of hydrogen gas per mole of carbon monoxide. One way of dealing with the excess hydrogen is to inject carbon dioxide into the methanol synthesis reactor, where it, too, reacts to form methanol according to the equation.

6. Glycerine[22,23]

Glycerol (glycerol/).[6] also called glycerine in British English and glycerine in American English, is a simple polyol compound. It is a colourless, odourless, viscous liquid that is sweet-tasting and non-toxic. The glycerol backbone is found in lipids known as glycosides. Due to having antimicrobial and antiviral properties it is widely used in FDA approved wound and burn treatments. Conversely, it is also used as a bacterial culture medium.[7]

Properties

- Chemical formula: - $C_3H_8O_3$
- Molar mass: - 92.094 $g.mol^{-1}$
- Appearance: - Colourless hygroscopic liquid
- Odour: - Odourless
- Density: - 1.261 g/cm3
- Melting point: - 17.8 °C (64.0 °F; 290.9 K)
- Boiling point-290 °C (554 °F; 563 K)[5]
- Solubility in water-miscible[2]
- Log P--2.32
- Vapor pressure-0.003 mmHg (50 °C)[2]
- Magnetic susceptibility (x)--57.06-10-6 cm3/mol
- Refractive index (nD) -1.4746
- Viscosity-1.412 Pats (20 °C)[4]

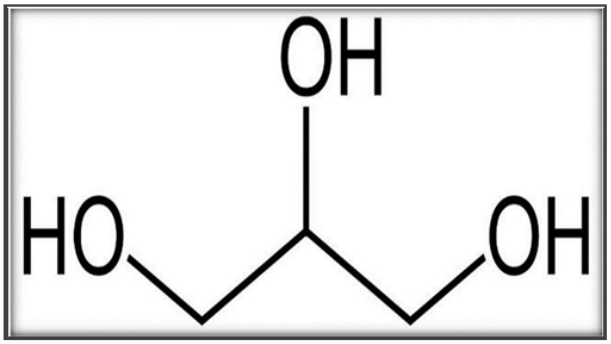


Fig No.9: - Structure of Glycerine.

Structure

Although achiral, glycerol is prochiral with respect to reactions of one of the two primary alcohols. Thus, in substituted derivatives, the stereospecific numbering labels the molecule with a "sn-" prefix before the stem name of the molecule.

Metabolism

Glycerol is a precursor for synthesis of triacylglycerols and of phospholipids in the liver and adipose tissue. When the body uses stored fat as a source of energy, glycerol and fatty acids are released into the bloodstream. Glycerol is mainly metabolized in the liver. Glycerol injections can be used as a simple test for liver damage, as its rate of absorption by the liver is considered an accurate measure of liver health. Glycerol metabolism is reduced in both cirrhosis and fatty liver disease. Blood glycerol levels are highly elevated during diabetes, and is believed.

Blood glycerollevels in diabetic patients average three times higher than healthy controls. Direct glycerol treatment of testes has been found to cause significant long-term reduction in sperm count. Furthertesting on this subject was abandoned due to the unexpected results, as this was not the goal of theexperiment. Circulating glycerol does not glycate proteins as do glucose or fructose, and does not lead to the formation of advanced glycation end products (AGES). In some organisms, the glycerol component can enter the glycolysis pathway directly and, thus, provide energy for cellular metabolism (or, potentially, be converted to glucose through gluconeogenesis).

Before glycerol can enter the pathway of glycolysis or gluconeogenesis (depending on physiological conditions), it must be converted to their intermediate glyceraldehyde 3- pHospHatein the following steps:

Physical Properties of Glycerine

Physically, glycerine or glycerol is soluble, nearly odourless, clear, viscous, hygroscopic liquid with a very high boiling point. The boiling point of pure alcohol at gas pressure (760 mm) is 290 degrees C.

Uses of Glycerine

1. In the food industry as a sweetener and preservative.
2. In liqueurs as a thickening agent.
3. It is not uncommon for glycerin to be in use as a filler in low-fat food item Such ascookies as a filler.
4. In the pharmaceutical and medical industries as a lubricant and humectant. It is moderatelyantimicrobial and antiviral and can therefore be used for wound treatment.
5. For the treatment of severely increased eye pressure.
6. Owing to its moisturizing properties, glycerin is in use within many skin-care
7. products that help prevent dry skin.
8. In the pharmaceutical industry for the preparation of cough syrups and other medicines. It is an important component of many skincare products. It is also in use for the productionof toothpaste. This compound does not nourish the plaque- forming bacteria that produce dental cavities.
9. In the production of electronic cigarette liquid.
10. explosives such as dynamite.
11. $C_3H_8O_3$ is used as fill to damp the vibrations in pressure gauges.
12. In film industries, to avoid the quick drying of wet areas and workspaces.
13. In use to protect some forms of plant leaves, glycerol and water can be used.
14. In explosives such as dynamite.
15. $C_3H_8O_3$ is in use as fill to damp the vibrations in pressure gauges.
16. In film industries, to avoid the quick drying of wet areas and workspaces.
17. In use to protect some forms of plant leaves, glycerol and water can be used.

Natural release Retardant

7. Banana peel extract

Herbal medicines have been used by the mankind since time immemorial. Ayurveda, the oldest traditional system of India, reveals that ancient Indians had a rich knowledge of medicinal value of different plants. India has been endowed with a very rich flora owing to the extreme variations in climate and geographical conditions prevalent in the country. With the advent in science, many of the crude drugs used in traditional system have been investigated scientifically. Musa paradisiaca Linn., known as Kadali in sanskrit is a highly valued medicinal plant widely used in Indian traditional system of medicine for curing various ailments.[1] In this review a comprehensive account of the morphology, phytochemical constituents, traditional uses, pharmacological activities and toxicity study are included in view of the many recent findings of importance on this plant.

Taxonomic Classification[2]

- Kingdom : Plantae Subkingdom :
- Tracheobionta Superdivision :
- Spermatophyta Division : Magnoliophyta
- Class : Liliopsida
- Subclass : Zingiberidae
- Order : Zingiberales
- Family : Musacea Genus : Musa LSpecies : M. paradisiaca L.

Synonyms[3] -Musa sapientum L., M. paradisiaca L. var sapientum (L) Kuntze, Plantain Vernacular names

- Sanskrit :Vana laxmi, Kadali,
- Rambha (unripe), Mochaka
- English : Plantain or Banana
- Hindi : Kela
- Maharashtrian : kela
- Gujarati : Keda
- Sindhi : Kewiro
- Telugu : Kadalamu,
- Ariti Tamil : Kadali Malayali :
- Vasha Konkan : Kelz

Flowering and Fruiting time: Throughout the year Parts Used: Fruit, leaves and stems. peels

Taxonomic and Genomic Classification[4-6]

Carolus Linnaeus, initially, classified banana into two species based on the pattern of consumption: Musa sapientum for dessert and Musa paradisiaca for plantains. The classification is based on chromosome numbers and morphological characters which is widely accepted by most of the taxonomists. Musa paradisiaca is a hybrid clone of Musa acuminata and Musa balbisiana. Cultivated bananas may be classed under 6 groups, each designated by letters which indicate their ploidy and genomic composition with respect to the two parent species (A for Musa acuminata and B for Musa balbisiana). Thus, AA and AAA (Musa sapientum) are diploid and triploid varieties of Musa acuminata. AB, AAB (Musa paradisiaca) and ABB are diploid and

triploid varieties of Musa balbisiana. Swennen (1990)

Occurrence and Distribution[7, 8]
It is a perennial herb growing 10-40 feet in height (look like tree) commonly found in the tropical and subtropical area. It occurs in all tropical areas native to India and Burma. In India, it is mostly found in Tamil Nadu, Andhra Pradesh, Bihar, Madhya Pradesh, West Bengal, Maharashtra, and Gujarat. It is also distributed in New Guinea, America, Australia and tropical Africa. Cultivation is limited to Florida, The Canary Islands, Egypt, Southern Japan, South Brazil.

Morphology Habit: Musa paradisiaca is one of the tallest herbaceous plant (up to 9 m long) with thick rhizome, pseudostem fleshy, succulent formed by the imbricate leaf sheaths.

Leaves: Large, oblong, petioles long channeled, bright glossy green.

Inflorescence: Spadix.

Flowers: Flowers on recurved large, spadix drooping, the lower flowers all female, the upper all male, clustered and enclosed in the axils of large, reddish purple caduceus, boat-shaped spathes or bracts. Calyx spathaceous, 5-toothed, white, corolla oblong, truncate, toothed, convolute round the stamens and style. Stamens 5 perfect and 1 small rudimentary or 0, filaments long stout, anthers linear, 2-celled. Ovary inferior, 3-celled, style long, stigma lobulate. **Fruit**: Berry, fleshy, narrow at both ends, seeds rarely present in cultivated variety. Outer region of fresh fruits are greenish, shiny and mucilaginous; rough and black when dry and inner region white, hard, powdery with less or without seeds.

Microscopy Flower[9-11] Powder of flower of M. paradisiaca contains fibro-vascular tissues, groups of pigmented lignified cells containing starch grains, epidermal tissues with stoma, prism like calcium oxalate crystals, and spherical pollen grains. Pigmented and non-pigmented sclerids, glandular trichomes, parenchyma of floral stalk and epidermal tissue with surface view are also present. Bract reveals the presence of spiral vessels with phloem fibres, blackish-brown pigmented thick-walled cells with spiral vessel and epidermal tissues with stomata, epidermal tissues with lateral view and epidermal cells with mesophyll tissues containing chloroplast. fibro-vascular tissues, parenchymatous tissues, groups of sclerids, bundle of simple phloem fibres, calcium oxalate crystals, nonglandular trichomes and part of annual vessels along with group of xylem fibres are also present. The adaxial epidermis of bracts of M. paradisiaca cultivars was glabrous and numerous paratetracytic, brachyparatetracytic and brachyparahexacytic-monopolar stomata. Rhaphide idioblast and inclusive bundle were absent from the adaxial epidermis of the bract as they seen in M.sapientum. Papillae were absent from the abaxial epidermis in M. paradisiaca while it observe in M. sapientum. Large and flattened fiber vascular tissues, small segment of pigmented sclereids, calcium oxalate crystal with prism- like structure were found in the powder stamen of M. paradisiaca. The ovary of M. paradisiaca is trilocular containing two seeds in each locule.

Powder also contains thick-walled parenchyma with simple trichome, Sieve tube with phloem parenchyma, fragments of sieve tubes, spiral vessels and thin walled pigmented sclerids.

Banana Peel
A banana peel, called banana skin in British English, is the outer covering of a banana. Banana peels are used as food for animals, an ingredient in cooking, in water purification, for manufacturing of several biochemical products as well as for jokes and comical situations. There are several methods to remove a peel from a banana.

Banana peels contain various compounds that can potentially enhance patch binding, particularly due to their fiber, pectin, and phenolic content. These components contribute to adhesive properties and can be leveraged in developing bio-based adhesives and composite materials.

- **Fiber**

Banana peels are rich in cellulose, hemicellulose, and pectin, which are all types of dietary fiber. These fibers can act as binding agents, increasing the cohesion and adhesion of materials.

- **Pectin**

Specifically, pectin, a type of polysaccharide, is known for its gelling and adhesive properties. It can be extracted and used as a natural binder.

- **Phenolic Compounds**

Banana peels contain various phenolic compounds, including catechols, flavanones, and flavanols. These compounds can interact with other materials, enhancing adhesion and providing antioxidant properties.

- **Starch**

Banana peels also contain starch, which can be extracted and used as a binder in composite materials. The starch, particularly amylopectin, contributes to flexibility and binding.

- **Minerals**

Banana peels are a good source of minerals like potassium and calcium, which can also play a role in binding and material properties.

How Banana Peels Can Enhance Patch Binding

- **Bio-based Adhesives**

Banana peel extracts, rich in pectin and phenolic

compounds, can be used to create bio-based adhesives. These adhesives can be used to bind various materials, offering a sustainable alternative to synthetic adhesives.

- **Composite Materials**

Banana peels can be incorporated into composite materials to improve their mechanical properties and binding characteristics. For example, banana peel powder can be mixed with other materials like cassava starch and banana stem fiber to create bio-composite sheets with enhanced strength and biodegradability.

Reinforcement: The cellulose and other fibers in banana peels can act as reinforcement agents in composite materials, increasing their tensile strength and resistance to tearing or breaking.

Improved Adhesion

The phenolic compounds and pectin in banana peels can interact with other materials, increasing their surface adhesion. This can be particularly useful in applications where patches or layers need to be firmly attached.

Example Applications:

Concrete Reinforcement

Banana peels can be used to reinforce concrete, improving its strength and durability.

Food Packaging

Banana peel extracts can be used to develop edible films and coatings for food packaging, improving shelf life and reducing reliance on plastic packaging.

Textile Industry

Banana peel extracts can be used to improve the binding of dyes and finishes on textiles, enhancing their colour fastness and durability. The nutritional value of banana peel depends on the stage of maturity and the cultivar; for example, plantain peels contain less fibre than dessert banana peels, and lignin content increases with ripening (from 7 to 15% dry matter). On average, banana peels contain 6-9% dry matter of protein and 20-30% fibre (measured as NDF). Green plantain peels contain 40% starch that is transformed into sugars after ripening. Green banana peels contain much less starch (about 15%) when green than plantain peels, while ripe banana peels contain up to 30% free sugars.

Fig. No. 10: - Structure of Banana Peel.

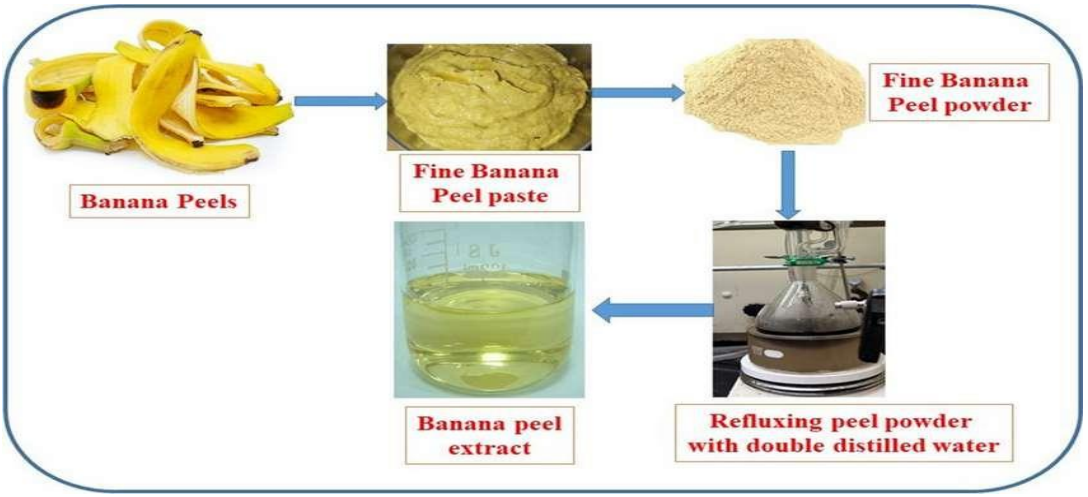


Fig. No. 11: - Processes of extraction.

Below image is attached to example the processes of formation of banana peel extract. sapientum. Papillae were absent from the abaxial epidermis in M. paradisiaca while it observe in M. sapientum. Large and flattened fiber vascular tissues, small segment of pigmented sclereids, calcium oxalate crystal with prism-like structure were found in the powder stamen of M. paradisiaca. The ovary of M. paradisiaca is trilocular containing two seeds in each locule. Ovary is covered with thick ovary wall, possessing multiple layer of outer cell. Prism like calcium oxalate crystals, fragments of xylem fibers, groups of thick-walled sclerenchyma and thick-walled parenchyma containing calcium oxalate crystals are reported in the transverse section of floral stalk. Powder also contains thick-walled parenchyma with simple trichome, Sieve tube with phloem parenchyma, fragments of sieve tubes, spiral vessels and thin walled pigmented sclerites.

Bark The transverse section of bark of M. paradisiaca showed that the epidermal cells are covered with cuticle. 2-3 hypodermal layers were found after epidermis. Different size groups of vascular bundle capped with sclerenchyma cell were observed.

Fruit Transverse section of unripe fruit of M. paradisiaca shows outer single layer epidermis made up of rectangle shaped parenchyma covered with thin cuticle papillae like outer protrution from each cell. Followed by epidermis, thick walled, irregular shaped, compactly arranged parenchymatous cells loaded with oval starch granules are present. Sclerenchymatous cells arranged in groups encircled with thin-walled parenchymatous cells, tannin cells and vascular bundles scattered in this region. Presence of 10-14 layers of compactly arranged parenchymatous cells are arranged longitude way. Mesocarp showed loosely arranged, tangentially elongated parenchymatous cells with abundant oval starch grains, raphide bundles with needle shaped crystals and few longitudinally extended parenchymatous cells with tannin cells. Powder study of fruit showed fragment of epidermal cells with papillae, different shape parenchymatous cells, Sclerenchymatous cells, reticulate helical vessels in groups, xylem cells in surface view, tannin cells, and abundant oval starch grains in groups.

Phytochemistry Flower

Dopamine, dopa, noradrenalin, serotonin, caffeic, cinnamic, p-coumaric, ferulic, gallic and protocatechuic acids, campesterol, b-sitosterol, stigmasterol, cyclomusalenol, cyclomusalenone were reported in flower.[12] Datta et al., isolated a tetracyclic triterpene named (24R)-4α·-14α·, 24 trimethyl-5 α -cholesta-8, 25(27)-dien-3β-ol from the flowers.[13] Martin et al., isolated a new hemiterpenoid glucoside named 1,1-dimethylallyl alcohol β- glucoside together with 3 known compounds, benzyl alcohol glucoside, syringin and (6S, 9R) roseoside from flower buds of Musa paradisiaca.[14] Anthocyanins Cyanidin-3-rutinoside, 3- rutinoside derivatives (dephinidin, pelargonidin, peonidine and malvidin) and anthocynidins (delphinidin, cyanidin, petunidin, pelargonidin, peonidin and malvidin) as potential food colorants were isolated from banana bracts.[15] Phytochemicals studies on banana flower extracts showed the presence of alkaloids, glycosides, steroids, saponins, tannins, flavonoids and terpenoids.[16] Onyenekwe et al., reported presence of tannins and glycosides in abundance while saponins, flavonoids, alkaloids, polyphenols and reducing sugars in moderate amounts in the aqueous stem extract.[17] Mishra et al., reported presence of alkaloids, carbohydrates, saponins, tannins, and phenols in aqueous and methanolic extracts of stamen.

Leaf -Baijal et al., studied the activities of starch phosphorylase, β-amylase, phosphohexoisomerase, acid and alkaline invertase, sucrose synthetase, sucrose phosphate synthetase and acid and alkaline phosphatase in various parts of the banana plant, using homogenates prepared in media supplemented with polyvinylpyrrolidone or Triton X-100. The results indicated that the supplement of choice depended on the enzyme and the tissue under study.[26] Shukla et al., reported variations in the activities of enzymes involved

in carbohydrate metabolism between different parts of the banana plant (Musa paradisiaca). Sucrose synthetase is present in the highest concentration in rootstock and fruit pulp, and sucrose phosphate synthetase in the pseudostem. The highest ratio of the activity of sucrose phosphate synthetase to sucrose synthetase is found in leaves. Acid invertase is present in leaves, leaf- sheath and fruit pulp and is not demonstrable in rootstock and pseudostem. Neutral invertase activity is high in pseudostem and leaf-sheath. Starch phosphorylase is largely concentrated in fruit pulp and rootstock. The maximum activity of ATPd isomerase is most active in the rootstock and lowest in the leaves.[27] Kumar and Sanwal isolated two forms (A and B) of starch phosphorylase were found in the mature banana electrophoresis leaf by polyacrylamide gel and DEAE-cellulose chromatography. The young leaf contained only form A and the appearance of form B with leaf development was accompanied by a decrease in the content of form A. At a later stage of leaf maturity only form B could be found. The MWs of forms A and B were 450 000, and 220 000 respectively.[28] Cemaluk et al., reported higher protein content, fat, crude fiber and ash in the ground leaves than that in the peels. Higher carbohydrate and moisture were recorded in the peels than in the leaves.

Traditional Uses Root is anthelmintics, antibailout and a valuable alterative. Juice of tender root is used in hemorrhage. It is also used in anemia and Cachexia. Root juice is used for urine retention, gonorrhea, bronchocele and strumous affections. Flowers are Astringent. Cooked flowers are used in diabetes. Juice of flowers mixed with curds used in dysmenorrhea and Menorrhagia. Juice of stem is used in otalgia and hemoptysis. Ripe fruit is Laxative (fully ripe fruit taken in early mornings), emollient, demulcent and nutrient. Unripe fruit is cooling, astringent, and antiscorbutic (in dry state) and used in diabetes, diarrhea and dessert. Flour of green plantain is used as chapatis in cases of dyspepsia with flatulence and acidity. Leaf is used as cool dressing to denuded wound and blisters.

Reported Pharmacological Activities Analgesic activity Hallikeri et al., also reported antinociceptive activity of corm extract of M. paradisiaca cv Puttabale in acetic acid induced writhing test, tail-flick test and hot plate test.[30] Gupta et al., reported that the aqueous extract of M. paradisiaca (250 mg/kg, 1000mg/kg, p.o.) showed significant analgesic activity in the experimental models (hot-plate method and writhing method) of rats.[31]

Antidepressant Activity Parle and Malik reported significant antidepressant potential of Musa paradisiaca fruit paste (5%, 10% and 20% w/w once daily for 15 successive days) in forced swim test and tail suspension test. Baclofen (10 mg/kg, i.p.), prazosin (62.5 mg/kg, i.p.) and p- CPA (100 mg/kg, i.p.) significantly antagonized this reduction in immobility time. levels. These findings reveal the anti-depressant potential of banana fruit appears to be related to anti-oxidant, pro adrenergic, pro-serotonergic and/ or Monoamine oxidase inhibitory activity exhibited by the banana fruit.[32] Darji and Galani also reported significant reduction of the immobility time with 14 days treatment of hydroalcoholic extract of Musa paradisiaca fruit (250 and 500 mg/kg, p.o.) in the forced swim test and tail suspension test. Antidepressant potential of the fruit extract was reduced by Haloperidol (0.1 mg/kg, i.p.) and increased by Bromocriptine mesylate (2 mg/kg, i.p.). The neurochemical estimation revealed the level of norepinephrine, dopamine and serotonin were increased with 14 days fruit extract treatment.[33]

Adaptogenic activity Ittiyavirah and Anurenj studied antistress activity of acetone extracts of unripe fruit peels and ripe fruit peels acetone extracts of M. paradisiaca in stress induced depression, chronic variable stress and anoxia stress models of animal and result indicated significant antistress activity of unripe fruit peel extract in stress induced depress model while both extracts showed protective effect in other two models.[34]

Anticonvulsant and CNS depressant activity Hallikeri et al., reported that corm extract of M. paradisiaca cv. Puttabale containing total phenolics (628.6 µg/mg) and flavonoids (321.6 µg/mg) caused a significant reduction of Maximal electroshock induced convulsions, Pentylenetetrazole induced convulsions and locomotor activity. The extract also reduced the reaction time of forced swim test and muscle coordination test. The results suggest that the corm extract of M. paradisiaca cv. Puttabale possess anticonvulsant, and CNS depressant properties which may be attributable to the presence of phenolics and flavonoids in the plant.[30]

Antidiarrhoeal Activity Yakubu et al., reported antidiarrhoeal activity of sap of M. paradisiaca (0.25, 0.50, and 1.00ml) in the castor oil-induced diarrhoea, castor oil-induced enteropooling, and gastrointestinal motility models of rats. The sap significantly prolonged the onset time of diarrhoea, decreased the number, fresh weight, and water content of feaces, and increased the inhibition of defecations. The antidiarrhoeal activity of Musa paradisiaca.

Antiulcerative Activity Elango et al., studied antiulcer activity of a siddha drug-ripe fruit Musa paradisiaca bhasma in rats in which ethanol (80%) induced acute ulcer model and acetic acid induced chronic ulcer model. The bhasma was administered in the dose of 10 and 20 mg/kg orally 1 hour prior to ulcer induction in acute model and administered daily for period of 10 days in chronic model. The antiulcer activity of the bhasma was indicated by significant reduction of the ulcer index and rise in mucin content. Antioxidant activity was also observed by estimation of catalase, superoxidase dismutase, lipid peroxidation.[40]

Antimicrobial Activity reported anti-microbial activity of aqueous extract of unripe fruit peels and leaves of Musa paradisiaca against Staphylococcus and Pseudomonas species in dehydrogenase assay. The fruit peel extract showed better activity against both bacteria than leaf extract, while the peel extract was more active against Staphylococcus (gram-positive) than Pseudomonas species (gram-negative).[42] However, Ahmad and Beg reported that alcoholic extract of Musa paradisiaca stem showed no activity against Staphylococcus aureus, Salmonella paratyphi, Shigella dysenteriae, Escherichia coli, Bacillus subtilis, and Candida albicans.[43] extracts exhibited antimicrobial activity with minimum inhibitory concentrations ranging from 5.62–25.81 and 7.60–31.50 µg/mL respectively.[45]

Antidiabetic Activity Ojewole and Adewunmi reported significant hypoglycemic effect of methanolic extract of mature, green fruits of Musa paradisiacal (100-800 mg/kg p.o.) in normal and streptozotocin -treated, diabetic mice.[50] The Ethanol and Ethanol: water (1:1) extracts of M. paradisiaca flowers were administered to normal and alloxan induced diabetic rats. The blood glucose levels were measured daily after oral administration of extracts at doses of 100, 250 and 500 mg/(kg.d). Both the extracts reversed the permanent hyperglycemia within a week in alloxan induced diabetic rats. The EtOH extract (250 mg/kg) was found to be 7.69% more potent hypoglycemic effect than standard oral hypoglycemic drug, glibenclamide 0.2 mg/kg b.w., respectively.[45]

Ahmad et al., measured the ability of the Musa paradisiacal tepal, flesh and skin extracts to scavenge free radicals using 2, 2-diphenyl-1- pcrylhydrazyl radical using quercetin as a reference radical scavenger Tepal methanol extract of was found to have the highest radical scavenging activity compared to others, such as tepal ethanol, tepal aqueous, skin methanol, flesh methanol and pure syringin. The IC 50 value of the tepal methanol extract was found to be 22.5 µg/ml. The highest total phenolic contents (expressed as microgram of Gallic acid equivalent per gram of the extracts) were found in tepal methanol extract (8000 µg/g) and the least in Flesh methanol extract (2150 µg/g).[57]

Antilipidemic Activity Usha et al., studied effect of neutral detergent fiber from Musa paradisiaca on cholesterol metabolism. Rats fed neutral detergent fiber from unripe banana showed significantly lower levels of cholesterol and triglycerides in serum and tissues in both cholesterol diet and cholesterol free diet groups when compared to control rats fed fiber free diets. However, neutral detergent fiber from the ripe fruit had no such effect. Concentration of hepatic bile acids and fecal excretion of neutral sterols and bile acids were more in rats fed neutral detergent fiber from unripe banana in both groups. Absorption of glucose and cholesterol in rabbits was significantly lowered only in presence of neutral detergent fiber from unripe banana.[58]

Antihypertensive Activity Osim et al., reported antihypertensive effect of ripe banana pulp (50 g/rat/day) in deoxycorticosterone enantate (DOC, 25 mg/rat) induced hypertensive rats. This effect may be due to the high tryptophan and carbohydrate content of banana that increases serotonin levels and gives serotonin-mediated natriorexic effect.[60] Orie reported that the effect of aqueous extract of plantain (Musa paradisiaca) showed concentration dependant hypotensive effect in both noradrenaline.

Cytotoxic and Thrombolytic Activity Chowdhury et al., reported significant cytotoxic and thrombolytic activity of methanol extract of Musa paradisiacal root by using brine shrimp lethality bioassay and in vitro clot lysis method respectively.[64]

Anti-Malarial Activity Bagavan et al., reported that ethyl acetate and methanol extract of Musa paradisiaca flower showed antimalarial activity against chloroquine (CQ)-sensitive (3D7) and CQ-resistant (Dd2 and INDO) strains of Plasmodium falciparum in culture using the luorescence-based SYBR Green assay.[65] Anbazhagan et al., tested silver nanoparticles (AgNP) of Musa paradisiaca stem extract were against larvae and pupae of the malaria vector Anopheles stephensi, with LC50 of 3.642 (I), 5.497 (II), 8.561 (III), 13.477 (IV), and 17.898 ppm (pupae), respectively. Furthermore, the antiplasmodial activity of nanoparticles was evaluated against chloroquine resistant (CQ-r) and chloroquine-sensitive (CQ-s) strains of Plasmodium falciparum, IC50 were 84.22 µg/ml (CQ-s) and 89.24 µg/ml (CQ-r), while chloroquine IC50 were 86 µg/ml (CQ-s) and 91 µg/ml (CQ-r).[66]

Hepatoprotective Activity Nirmala et al., investigated the hepatoprotective activity of alcoholic and aqueous stem extracts of Musa paradisiaca in CCl4 and paracetamol induced hepatotoxicity models in rats. Pretreatment with alcoholic extract (500 mg/kg), more significantly and to a lesser extent the alcoholic extract (250 mg/kg) and aqueous extract (500 mg/kg), reduced the elevated levels of the serum enzymes like serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase (ALP) and bilirubin levels and alcoholic and aqueous extracts reversed the hepatic damage towards the normal.[69]

Hair growth Promoting Activity Savali et al., tested the effect of aqueous and methanolic extract of M. paradisiaca unripe fruits for hair growth promoting activity by studying hair length and microscopic study of follicles in vehicle control, 2% minoxidil treated and extract treated animals. Animals treated with aqueous and methanolic extract of M. paradisiaca showed better efficacy as compared to the control and standard group suggests that it has potential as a hair growth promoter.[70]

Wound Healing Activity Amutha and Selvakumari tested the methanolic extract of Musa paradisiaca Linn. stem on the burn wound created by using red hot steel rod from above the hind limb region of wistar albino rats and the progressive changes in healing were monitored every day. The wound contraction rate was observed based on the histopathological.

Reproductive Activity Alabi et al., studied the effects of administration of mature green fruits of Musa paradisiaca powder dissolve in distilled water (500 mg/kg, 1000 mg/kg) on the semen quality of adult male Wistar rats. Significant increment in the semen parameters was noticed in animals that received a lower dose of the plantain flour, but those animals who received the high dose had marked and very significant reduction in sperm cell concentration and percentage of morphologically normal spermatozoa.[73] Yakubu et al., anana stalk (AABS).

Bioabosrptive Activity Raw banana stalk (RBS), acid activated b and base activated banana stalk (BABS) prepared by Ogunleye et al., from banana stalk were used as biosorbents to remove Lead(II) from aqueous solution. The biosorbents were characterized using proximate analysis and Fourier transform infraredspectroscopy. Pb(II) of 1000 mg/L concentration was prepared from Pb(NO3)2 salt and other concentrations were obtained from this stock through serial dilution. Effects of adsorbent dose, temperature, initial metal concentration, contact time and pH on the percentage Pb(II) removal were evaluated. The Pb(II) concentrations in the solutions were analysed using Atomic Absorption Spectrophotometer. At an equilibrium time of 180 minutes, the percentage Pb(II) removal was 63.97%, 96.13% and 66.90% for RBS, AABS and BABS, respectively.[75]

Tablet Disintegrant Activity Singh et al., evaluated the three varieties of Musa paradisiaca L. in their unripe state as tablet disintegrant while formulating Orally Disintegrating Tablet (ODT) and other fast disintegrating dosage forms that showed promising results as potential tablet disintegrant for hardness, friability, in vitro disintegration.

- **Refluxing for Extraction**

Refluxing is a process where the banana peel powder is boiled in a solvent (in this case, double distilled water) under controlled conditions, allowing for continuous extraction of the desired compounds. This method is effective in breaking down the peel material and releasing its soluble components.

8. Okra

Okra, also known as lady's finger, possesses properties that can be beneficial in a patch for natural release retardant. Specifically, ular in the Inokra mucilage, a viscous substance extracted from the plant, can be used as a natural polymer to control the release of active ingredients in patches and other drug delivery systems. Okra (Abelmoschus esculentus) is the only vegetable crop of significance in the Malvaceae family and is very popdo-Pak subcontinent. In India, it ranks number one in its consumption but its original home is Ethiopia and Sudan, the north- eastern African countries. It is one of the oldest cultivated crops and presently grown in many countries and is widely distributed from Africa to Asia, southern Europe and America. It is a tropical to subtropical crop and is sensitive to frost; low temperature, water logging and drought conditions, and the cultivation from different countries have certain adapted distinguishing characteristics specific to the country to which they belong1. It is an oligo purpose crop, but it is usually consumed for its green tender fruits as a vegetable in a variety of ways. These fruits are rich in vitamins, calcium, potassium and other mineral matters. The mature okra seed is a good source of oil and protein has been known to have superior nutritional quality. Okra seed oil is rich in unsaturated fatty acids such as linoleic acid, which is essential for human nutrition. Its mature fruit and stems contain crude fibre, which is used in the paper industry1.

Fig. No. 12: - Structure of Okra.

Description
Biological name: Hibiscus esculentus, Abelmoschus esculentus**.** Scientific classification: Kingdom: Plantae Division: Magnoliophyta Class: Magnoliopsida (Unranked): Rosids Order: Malvales.

Chemical composition: Okra bast, a multicellular fiber was analyzed and the estimated average chemical compositions of OBF (Abelmoschus esculentus variety) are 67.5 % a-cellulose, 15.4% hemicelluloses, 7.1 % lignin, 3.4 % pectic matter, 3.9 % fatty and waxy matter and 2.7 % aqueous extract. It is clear that the main constituents of OBF are a-cellulose, hemicelluloses and lignin and the rest are very minor in proportion, so render a little influence to the structure of OBF. Therefore, the structure of a-cellulose, hemicelluloses and lignin and the mode of combinations that exist in between themselves are dominating the structure of OBF.

Parts used: fruit, leave seed, root.
Medicinal uses: Plants for a future cannot take any responsibility for any adverse effects from the use of plants. Always seek advice from a professional before using a plant medicinally. Antispasmodic; Demulcent; Diaphoretic; Diuretic; Emollient; Stimulant; Vulnerary. The roots are very rich in mucilage, having a strongly demulcent action. They are said by some to be better than marsh mallow (Althaea officinalis). This mucilage can be used as a plasma replacement. An infusion of the roots is used in the treatment of syphilis. The juice of the roots is used externally in Nepal to treat cuts, wounds and boils. The leaves furnish an emollient poultice. A decoction of the immature capsules is demulcent, diuretic and emollient. It is used in the treatment of catarrhal infections, dysuria and stimulant. An infusion of the roasted seeds has sudorific properties. Other Uses: Fiber; Paper; A fiber obtained from the stems is used as a substitute for jute. It is also used in making paper and textiles. The fibers stripped off. The fibers are cooked for 2 hours with lye and then put in a ball mill for 3 hours. The paper is Cream colored. A decoction of the root or of the seeds is used as a size for paper.

21.Used for: Sylvia Zook, a qualified nutritional specialist, states that okra can favour one's body due to its properties: 1. Okra contains special fiber which takes sugar levels in blood under control, providing sugar quantity, acceptable for the bowels. 2. Mucilage, found in okra, is responsible for washing away toxic substances and bad cholesterol, which loads the liver 3. Purgative properties okra possesses are beneficial for bowel purification. Due to okra fiber content, sufficient water levels in faces are ensured. Consequently, no discomfort and constipation bothers the patient. Wheat bran, applied for this purpose, can impose certain irritation on the bowels, while okra makes it smooth and all convenient and safe for the user. Mucilage provides soft effect on the bowels. Stimulating bile movement, okra washes excess cholesterol and harmful substances from the body. This benefits the organism in general, as the toxins and bad cholesterol can induce various health conditions. Okra poses no threat to the organism, causes no addiction; it is completely safe and Reliable. Moreover, it contains a bunch of useful nutrients and is cheaper than chemical alternatives. 4. Fiber okra contains is a valuable nutrient for intestine microorganisms.

This ensures proper intestine functionality. 5. Okra ensures recovery from psychological and mental conditions, like, depression and general weakness. 6. Okra is an effective remedy for ulcers and joint healthiness. It is used counteract the acids, 7. Due to its alkaline origin. It also guards the mucous membranes of the digestive system, by covering them with additional layer.

8. Okra is additionally applied for pulmonary inflammations, bowel irritations, and sore throat. According to Indian researches, okra is a complex replacement for human blood plasma. In order to keep the valuable substances safe, it's necessary to cook okra as shortly as possible, processing it either with steam, or on low heat.

Okra mucilage, an acidic polysaccharide, contains galactose, rhamnose, and galacturonic/glucuronic acid. Its mucoadhesive properties stem from the presence of hydroxyl and carboxylic acid groups, potentially leading to sustained or controlled release profiles.

- **Improved Skin Adhesion**

The bioadhesive properties of okra mucilage can help the transdermal patch adhere better to the skin, ensuring consistent drug delivery over time

Natural Alternative
Okra mucilage offers a natural alternative to synthetic polymers, which may be preferred by some consumers and pharmaceutical companies.

- **Natural Polymer**

Okra mucilage is a natural, biocompatible, and biodegradable polymer, making it a suitable alternative to synthetic polymers in various applications, including controlled-release systems.

- **Viscous Nature**

When extracted in water, okra mucilage forms a highly viscous solution, which is crucial for retarding the release of active ingredients from a patch or other dosage form.

- **Drug Release Retardation**

The viscous nature of okra mucilage allows it to be incorporated into a patch formulation to create a matrix that controls the rate at which the active ingredient is released. This is particularly useful for creating sustained-release or extended-release patches.

- **Mucoadhesion**

Some studies suggest that okra mucilage-based formulations can also exhibit mucoadhesion, meaning they can adhere to mucosal surfaces, which can be advantageous for certain types of patches.

- **Potential for Wound Healing**

Okra mucilage has also shown potential in wound healing due to its anti-inflammatory and antimicrobial properties, making it potentially beneficial for patches designed for wound care.

- **Antimicrobial Properties**

Okra contains compounds like palmitic and stearic acids that exhibit antimicrobial effects, which could be helpful in preventing infection in wound-healing patches.

In essence, okra mucilage's unique properties make it a promising candidate for developing natural and effective controlled-release patches.

Preparation of Okra Mucilage Okra mucilage (OM) is a natural polysaccharide isolated from Hibiscus esculentus fruits, composed of D-galactose, L-rhamnose and L-galacturonic acid.12 Okra fruits were purchased from a local market; hence the seeds do not contain mucilage, were removed prior to extraction, sliced and macerated with five folds its weight of distilled water for 12 h. This was followed by filtration through muslin cloth, treated with 0.3 N Ba(OH)2 –5% aqueous ZnSO4 for deproteinization and centrifuged at 5000 g for 30 min. The mucilage was precipitated from the clear viscous supernatant with equal volume of ethanol, filtered, washed with excess ethanol followed by acetone and dried at 60ºC.13.

The okra fiber posses an excellent quantity of cellulose. Hence it can be used as cellulosic raw materials in cellulose based industries. It also contains low percentage of lignin, which is responsible for yellowing and photochemical degradation. it is a high molecular weight compounds. So it has some developed properties like colour fastness, tensile strength etc. in Philippines OBF is used as textile fiber. It is also having excellent anti oxidant activity and memory enhancement activity. If we collect and properly use the okra bast by isolating fiber from it then a good prospect must be await for our country and also we can use this extract as a good medicine for alzhemeirs disease.

The fruits of Abelmoschus esculentus (Okra) are consumed as food not only in Turkey but also in many parts of the world. The fruits with abundant mucilage have been used for many years in traditional medicine to treat gastric lesions and inflammatory diseases. In the study conducted, the total antioxidant capacity in aqueous and ethanolic extracts of okra fruit differs according to the literature. These different effects are thought to be due to the diverse antioxidant potentials of the aqueous and ethanolic extracts. Previously different parts of the okra plant, such as the fruit or the seed, have also been reported to possess various activities. In the present study, it is aimed to get higher activity potential, and therefore whole fruit, including the seeds, are extracted together. The literature has previously stated that the variations, particularly in the polyphenolic and flavonoid contents, may be due to the cultivation conditions, harvesting time of the plant or the climatic conditions of the concerned region. In our study, it is shown that the ethanolic extract of Kilis origin fruits has a very high phenolic content. It is known that geographical location is also an influencing factor in terms of lipid, fatty acid and amino acid compositions. Furthermore.

9. Dimethyl sulfoxide (DMSO)

Dimethyl sulfoxide (DMSO) is widely recognized as a powerful skin penetration enhancer in topical drug delivery. DMSO increases the absorption of various drugs through the skin, making it a valuable tool for improving the effectiveness of transdermal therapies.

Mechanisms of Action

- **Disruption of Skin Barrier:** DMSO interacts with both the protein (keratin) and lipid components of the stratum corneum, the skin's outermost layer, altering their structure and organization to reduce barrier resistance and facilitate drug passage.

- **Solvent Properties:** DMSO acts as a solvent, increasing drug solubility and partitioning into the skin, which further enhances penetration.

Effectiveness as a Penetration Enhancer

- **Broad Drug Applicability:** DMSO has been shown to enhance the skin absorption of a wide range of drugs, including heparin, estradiol, medroxyprogesterone acetate, celecoxib, ketorolac tromethamine, and tadalafil
- **Magnitude of Enhancement:** Studies report significant increases in drug flux—up to 4- to 4.5-fold higher—when DMSO is included in topical formulations compared to controls without DMSO **3410**.
- **Concentration-Dependent Effects:** Higher concentrations of DMSO generally lead to greater enhancement, but optimal levels must be balanced to avoid potential skin irritation.
- The 'drug-in-adhesive' type patches (DIA) consist of a matrix polymer, which is typically dissolved together with the active in an organic solvent mixture to allow their formulation as a liquid and castable drug-in-adhesive mass. However, by the end of the production cycle, those solvents must be eliminated from the liquid mass to enable the curing of the drug-containing adhesive mix. Insufficient solvent evaporation would inhibit the formation of the solid DIA- structure on one hand, and create toxicological issues on the other. Accordingly, it is a major challenge to incorporate a volatile permeation

enhancer that could increase permeated drug amount and simultaneously stabilize the supersaturated patch matrix from drug recrystallization while evaporating the matrix polymer solvents to solidify the patch. Here, we report on the feasibility of a DMSO-containing DIA based on duro-tak

- **Names**
- **Preferred IUPAC name** (Methanesulfinyl)methane
  Systematic IUPAC name

(Methanesulfinyl)methane (substitutive) Dimethyl (oxido) sulfur (additive)
Other names
Methylsulfinylmethane
Methyl sulfoxide (2:1), Dermasorb[1]
Identifiers
Abbreviations DMSO, Me2SO

Table No. 3: Properties of DMSO.

Properties	
Chemical formula	$(CH_3)_2SO$
Molar mass	78.13 $g \cdot mol^{-1}$
Appearance	Colourless liquid
Density	1.1004 $g \cdot cm^{-3}$
Melting point	19 °C (66 °F; 292 K)
Boiling point	189 °C (372 °F; 462 K)
Solubility in water	Miscible
Solubility in Diethyl ether	Not soluble
Vapor pressure	0.556 millibars or 0.0556 kPa at 20 °C[2]
Acidity (pK_a)	35[3]
Refractive index (nD)	1.479 ε_r = 48
Viscosity	1.996 cP at 20 °C

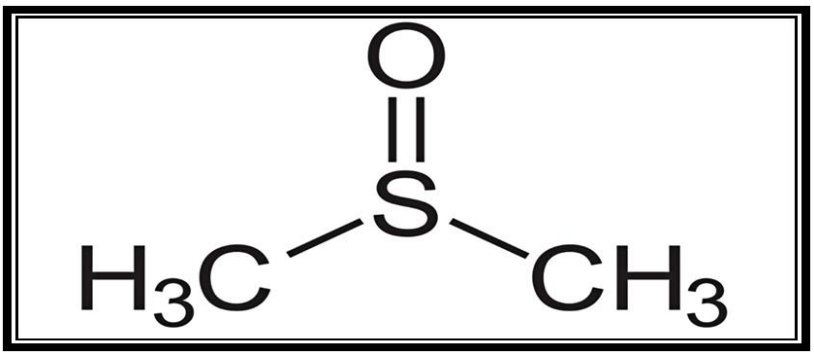


Fig No. 13: - Structure of DMSO.

- **Structure**

Point group	C_s
Molecular shape	Trigonal pyramidal
Dipole moment	3.96 D

Dimethyl sulfoxide (DMSO) is an organosulfur compound with the formula (CH3)2S=O. This colorless liquid is the sulfoxide most widely used commercially. It is an important polar aprotic solvent that dissolves both polar and nonpolar compounds and is miscible in a wide range of organic solvents as well as water. It has a relatively high boiling point. DMSO is metabolized to compounds that leave a garlic-like taste in the mouth after DMSO is absorbed by skinIn terms of chemical structure, the molecule has idealized Cs symmetry. It has a trigonal pyramidal molecular geometry consistent with other three-coordinate S(IV) compounds, with a nonbonded electron pair on the approximately tetrahedral sulfur atom.

Synthesis and production
Dimethyl sulfoxide was first synthesized in 1866 by the Russian scientist Alexander Zaytsev, who reported his

findings. Its modern use as an industrial solvent began through popularization by Thor Smedslund at the Stepan Chemical Company. Dimethyl sulfoxide is produced industrially from dimethyl sulfide, by-product of the kraft process, by oxidation.

Reactions with electrophiles

The sulfur center in DMSO is nucleophilic toward soft electrophiles and the oxygen is nucleophilic toward hard electrophiles. With methyl iodide it forms trimethylsulfoxonium iodide, [(CH3)3SO]+I−:

(CH3)2SO + CH3I → [(CH3)3SO]I

This salt can be deprotonated with sodium hydride to form the sulfur ylide: [(CH3)3SO]I + NaH → (CH3)2S(CH2)O + NaI + H2

Acidity

The methyl groups of DMSO are only weakly acidic, with a pKa = 35. For this reason, the basicities of many weakly basic organic compounds have been examined in this solvent.[10] Deprotonation of DMSO requires strong bases like lithium diisopropylamide and sodium hydride. Stabilization of the resultant carbanion is provided by the S(O)R group. The sodium derivative of DMSO formed in this way is referred to as dimsyl sodium. It is a base, e.g., for the deprotonation of ketones to form sodium enolates, phosphonium salts to form Wittig reagents, and formamidinium salts to form diaminocarbenes. The dimsyl anion is a potent nucleophile.

Ligand and Lewis base

Main article: Transition metal sulfoxide complex

Related to its ability to dissolve many salts, DMSO is a common ligand in coordination chemistry. Illustrative is the complex dichlorotetrakis(dimethyl sulfoxide)ruthenium(II) (RuCl2(dmso)4). In this complex, three DMSO ligands are bonded to ruthenium through sulfur. The fourth DMSO is bonded through oxygen. In general, the oxygen-bonded mode is more common. In carbon tetrachloride solutions DMSO functions as a Lewis base with a variety of Lewis acids such as I2, phenols, trimethyltin chloride, metalloporphyrins, and the dimer Rh2Cl2(CO)4. The donor properties are discussed in the ECW model. The relative donor strength of DMSO toward a series of acids, versus other Lewis bases, can be illustrated by C-B plots.DMSO is a polar aprotic solvent and is less toxic than other members of this class, such as dimethylformamide, dimethylacetamide, N-methyl-2-pyrrolidone, and hexamethyl phosphoramide (HMPA).

involving salts, most notably Finkelstein reactions and other nucleophilic substitutions. It is also extensively used as an extractant in biochemistry and cell biology. Because DMSO is only weakly acidic, it tolerates relatively strong bases and as such has been extensively used in the study of carbanions. A set of non-aqueous pKa values (C-H, O-H, S-H and N-H acidities) for thousands of organic compounds have been determined in DMSO solution.

Because of its high boiling point, 189 °C (372 °F), DMSO evaporates slowly at normal atmospheric pressure. Samples dissolved in DMSO cannot as easily be recovered compared to other solvents, as it is very difficult to remove all traces of DMSO by conventional rotary evaporation. One technique to fully recover samples is removal of the organic solvent by evaporation followed by addition of water (to dissolve DMSO) and cryodesiccation to remove both DMSO and water. Reactions conducted in DMSO are often diluted with water to precipitate or phase-separate products. The relatively high freezing point of DMSO, 18.5 °C (65.3 °F), means that at, or just below, room temperature it is a solid.

In its deuterated form (DMSO-d6), it is a useful solvent for NMR spectroscopy, again due to its ability to dissolve a wide range of analytes, the simplicity of its own spectrum, and its suitability for high-temperature NMR spectroscopic studies. Disadvantages to the use of DMSO-d6 are its high viscosity, which broadens signals, and its hygroscopicity, which leads to an overwhelming H2O resonance in the 1H-NMR spectrum. It can be mixed with CDCl3 or CD2Cl2 for lower viscosity and melting points.

DMSO is used to dissolve test compounds in in vitro drug discovery[19][20] and drug design[21] screening programs, including high-throughput screening programs.[20][21] This is because it is able to dissolve both polar and nonpolar compounds,[19][21] can be used to maintain stock solutions of test compounds (important when working with a large chemical library),[20] is readily miscible with water and cell culture media, and has a high boiling point (this improves the accuracy of test compound concentrations by reducing room temperature evaporation).[19] One limitation with DMSO is that it can affect cell line growth and viability, with low DMSO concentrations sometimes stimulating cell growth.

DMSO is used as a vehicle in in vivo studies of test compounds. It has, for example, been employed as a co-solvent to assist absorption of the flavonol glycoside icariin in the nematode worm Caenorhabditis elegans.[22] As with its use in in vitro studies, DMSO has some limitations in animal models. Pleiotropic effects can occur and, if DMSO control groups are not carefully planned, then solvent effects can falsely be attributed to the prospective drug.[23] For example, even a very low dose of DMSO has a powerful protective effect against paracetamol (acetaminophen)-induced liver injury in mice. DMSO finds some use in manufacturing processes to produce microelectronic devices. It is widely used to strip photoresist in TFT-LCD 'flat panel' displays and advanced packaging applications (such as wafer-level packaging / solder bump patterning).

Biology

DMSO is used in the polymerase chain reaction (PCR) to inhibit secondary structures in the DNA template or the DNA primers. It is added to the PCR mix before reacting, where it interferes with the self-complementarity of the DNA, minimizing interfering reactions.[26] DMSO in a PCR is applicable for supercoiled plasmids (to relax before amplification) or DNA templates with high GC-content (to decrease thermostability). For example, 10% final concentration of DMSO in the PCR mixture with Phusion decreases primer annealing temperature (i.e., primer melting temperature) by 5.5–6.0 °C (9.9–10.8 °F).[27] It is well known as a reversible cell cycle arrester at phase G1 of human lymphoid cells.[28]

DMSO may also be used as a cryoprotectant, added to cell media to reduce ice formation and thereby prevent cell death during the freezing process.[29] Approximately 10% may be used with a slow-freeze method, and the cells may be frozen at −80 °C (−112 °F) or stored in liquid nitrogen safely.[citation needed]In cell culture, DMSO is used to induce differentiation of P19 embryonic carcinoma cells into cardiomyocytes and skeletal muscle cells.

Medicine

Use of DMSO in medicine dates from around 1963, when an Oregon Health & Science skin and other membranes without damaging them and could carry other compounds into a biological system. In medicine, DMSO is predominantly used as a topical analgesic, a vehicle for topical application of pharmaceuticals, as an anti-inflammatory, and an antioxidant.[30] Because DMSO increases the rate of absorption of some compounds through biological tissues, including skin, it is used in some transdermal drug delivery systems. Its effect may be enhanced with the addition of EDTA. It is frequently compounded with antifungal medications, enabling them to penetrate not just skin but also toenails and fingernails.[31]

DMSO has been examined for the treatment of numerous conditions and ailments, but the U.S. Food and Drug Administration (FDA) has approved its use only for the symptomatic relief of patients with interstitial cystitis.[32] A 1978 study concluded that DMSO brought significant relief to the majority of the 213 patients with inflammatory genitourinary disorders that were studied.[33] In 2009, the first to obtain FDA approval for topical DMSO usage was PENNSAID®, which contains diclofenac in a carrier with 45.5% DMSO.

Each 1 mL of TDiclo contains 16.05 mg diclofenac sodium. TDiclo solution also contains 45.5% dimethyl sulfoxide (DMSO) vehicle, which can result in enhanced penetration of active drug through the skin. The most common adverse event reported was dry skin at the application site (25.3% of patients), followed by contact dermatitis (13.0%).[35]

In interventional radiology, DMSO is used as a solvent for ethylene vinyl alcohol in the Onyx liquid embolic agent, which is used in embolization, the therapeutic occlusion of blood vessels.[citation needed] In cryobiology DMSO has been used as a cryoprotectant and is still an important constituent of cryoprotectant vitrification mixtures used to preserve organs, tissues, and cell suspensions. Without it, up to 90% of frozen cells will become inactive. It is particularly important in the freezing and long-term storage of embryonic stem cells and hematopoietic stem cells, which are often frozen in a mixture of 10% DMSO, a freezing medium, and 30% fetal bovine serum. In the cryogenic freezing of heteroploid cell lines (MDCK, VERO, etc.) a mixture of 10% DMSO with 90% EMEM (70% EMEM + 30% fetal bovine serum + antibiotic mixture) is used. As part of an autologous bone marrow transplant.

DMSO is metabolized by disproportionation to dimethyl sulfide and dimethyl sulfone. It is subject to renal and pulmonary excretion. A possible side effect of DMSO is therefore elevated blood dimethyl sulfide, which may cause a blood borne halitosis symptom.

Alternative medicine

DMSO's popularity as an alternative medicine is stated to stem from a March 1980 60 Minutes documentary "The Riddle of DMSO"[36] and April 1980 Time magazine article[37] covering the treatments of ardent DMSO advocate Dr. Stanley Jacob beginning in the 1960s.[38]

The use of DMSO as an alternative treatment for cancer is of particular concern, as it has been shown to interfere with a variety of chemotherapy drugs, including cisplatin, carboplatin, and oxaliplatin.[39] There is insufficient evidence to support the hypothesis that DMSO has any effect,[40] and most sources agree that its history of side effects when tested warrants caution when using it as a dietary supplement,for which it is marketed heavily with the usual disclaimer. DMSO is an ingredient in some products listed by the U.S. FDA as fake cancer cures[41] and the FDA has had a running battle with distributors.[36] One such distributor is Mildred Miller, who promoted DMSO for a variety of disorders and was consequently convicted of Medicare fraud.

Veterinary medicine

DMSO is commonly used in veterinary medicine as a liniment for horses, alone or in combination with other ingredients. In the latter case, often, the intended function of the DMSO is as a solvent, to carry the other ingredients across the skin. Also in horses, DMSO is used intravenously, again alone or in combination with other drugs. It is used alone for the treatment of increased intracranial pressure and/or cerebral edema in horses.

Taste

The perceived garlic taste upon skin contact with DMSO may be due to nonolfactory activation of TRPA1

receptors in trigeminal ganglia.[43] Unlike dimethyl and diallyl disulfides (which have odors resembling garlic), mono- and tri- sulfides (which typically have.

Toxicity

DMSO is a non-toxic solvent with a median lethal dose higher than ethanol (DMSO: LD50, oral, rat, 14,500 mg/kg;[44][45] ethanol: LD50, oral, rat, 7,060 mg/kg.[46]).

DMSO can cause contaminants, toxins, and medicines to be absorbed through the skin, which may cause unexpected effects. DMSO is thought to increase the effects of blood thinners, steroids, heart medicines, sedatives, and other drugs. In some cases this could be harmful or dangerous.[47]

Because DMSO easily penetrates the skin, substances dissolved in DMSO may quickly be absorbed. Glove selection is important when working with DMSO. Butyl rubber, fluoroelastomer, neoprene, or thick (15 mil / 0.4 mm) latex gloves are recommended.[48] Nitrile gloves, which are very commonly used in chemical laboratories, may protect from brief contact but have been found to degrade rapidly with exposure to DMSO

Toxicology study

Considering its wide use, especially for cryopreservation and in vitro assays, we evaluated biological effect of DMSO using these technological innovations. We exposed 3D cardiac and hepatic microtissues to medium with or without 0.1% DMSO and analyzed the transcriptome, proteome and DNA methylation profiles. In both tissue types, transcriptome analysis detected >2000 differentially expressed genes affecting similar biological processes, thereby indicating consistent cross-organ actions of DMSO.

Regulation

In Australia, it is listed as a Schedule 4 (S4) Drug, and a company has been prosecuted for adding it to products as a preservative.

Clinical safety

Early clinical trials with DMSO were stopped because of questions about its safety, especially its ability to harm the eye. The most commonly reported side effects include headaches and On September 9, 1965, The Wall Street Journal reported that a manufacturer of the chemical warned that the death of an Irish woman after undergoing DMSO treatment for a sprained wrist may have been due to the treatment, although no autopsy was done, nor was a causal relationship established.[51] Clinical research using DMSO was halted and did not begin again until the National Academy of Sciences (NAS) published findings in favor of DMSO in 1972.[52] In 1978, the US FDA approved DMSO for treating interstitial cystitis. In 1980, the US Congress held hearings on claims that the FDA was slow in approving DMSO for other medical uses. In 2007, the US FDA granted "fast track" designation on clinical studies of DMSO's use in reducing brain tissue swelling following traumatic brain injury.[52]

DMSO exposure to developing mouse brains can produce brain degeneration. This neurotoxicity could be detected at doses as low as 0.3 mL/kg, a level exceeded in children exposed to DMSO during bone marrow transplant.[53]

Odor problem

DMSO disposed into sewers can cause odor problems in municipal effluents: waste water bacteria transform DMSO under hypoxic (anoxic) conditions into dimethyl sulfide (DMS) that has a strong disagreeable odor, similar to rotten cabbage.[54] However, chemically pure DMSO is odorless because of the lack of C-S-C (sulfide) and C-S-H (mercaptan) linkages. Deodorization of DMSO is achieved by removing the odorous impurities it contains.[55]

Explosion hazard

Dimethyl sulfoxide can produce an explosive reaction when exposed to acyl chlorides; at a low temperature, this reaction produces the oxidant for Swern oxidation.[citation needed]

DMSO can decompose at the boiling temperature of 189°C at normal pressure, possibly leading to an explosion. The decomposition is catalyzed by acids and bases and therefore can be relevant at even lower temperatures. A strong to explosive reaction also takes place in combination with halogen compounds, metal nitrides, metal perchlorates, sodium hydride, periodic acid and Fluorinatingagent.[56]

MATERIAL AND EQUIPMENT

Table No. 4: -Material and Equipment.

Sr .no	Name of the Instrument	Model / Manufacturer
1	Digital weighing balance.	Mettler Toledo
2	UV spectrometer.	Shimadzu(1900i)
3	Magnetic Stirrer.	Microtek
4	Sonicator	Lab hosp
5	Hot Air Oven	Lab hosp
6	Desiccator	Lab hosp
7	Digital pH meter	Equip – tronics
8	soxhlet extraction system	Lab hosp

1- Analytical weighing balance

Analytical weighing balance are used in laboratories to efficiently perform specific tasks such as weighing test materials and sampling amount, formulation, density, determination, purityanalysis, quality control testing and material and conformance testing.

2- UV Spectrometer

UV absorption spectroscopy is one of the best methods for determination of impurities in organic molecules. Additional peaks can be observed due to impurities in the sample and it can be compared with that of the standard raw material. By also measuring the absorbance at a specific wavelength, the impurities can be detected.

3– Magnetic stirrer

A magnetic stirrer is a device widely used in laboratories and consists of a rotating magnet or a stationary electromagnet that creates a rotating magnetic field. This device is used to make a stir bar, immerse or mix a solution.

4– Sonicator

Sonicators are high-frequency tools that use to ultrasonic energy to agitate particles in liquids. These devices are employed to facilitate to a wide variety of processes, such as mixing, cleaning, degassing, cell disruption and sample preparation.

5- Hot Air Oven

A hot air oven is used to sterilize the product in a particular period of time under specific condition like humidity, pressure, and other environmental factors. Hot air oven controls the humidity level by removing moisture from the products and combining the airflow with heat.

6– Desiccator

Desiccator are sealable enclosures containing desiccants used for preserving moisture- sensitive items such as cobalt chloride paper for another use. A common use for desiccators is to protect chemicals which are hygroscopic or which react with water from humidity.

7- Digital pH meter

pH meter is an instrument used to measure acidity or alkalinity of a solution also known as pH. pH is the unit of measure that describes the degree of acidity or alkalinity.

8-Soxhlet extraction system

Principle

The Soxhlet extraction method uses a small amount of solvent and is very cost-effective.

The Soxhlet extraction uses the solvent reflux and siphon principle to continuously extract the solid matter by pure solvent, which saves the solvent extraction efficiency and high efficiency. The sold sample is placed on a thimble-shaped filter paper, positioned into Soxhlet extractor, and the device is assembled. The solvent is added to the solvent reservoir flask and mounted onto a heating mantle. After heating, the condensed vapors of the solvent come in contact with the sample powder, and the soluble part of the powder gets mixed with the solvent for extraction.

When the solvent surface exceeds the maximum height of the siphon, the solvent containing the extract is siphoned back. The flask is repeated, extracting a portion of the material each time so that the solid material is constantly used as a pure solvent and the extracted material is concentrated in the flask.

Soxhlet extraction working

First of all, weight approximately 15-20g sample in filter paper. Please note that the sample should be in powder form. Close the filter paper and keep in the siphon tube Also, weight empty flask Adjust the apparatus like in the picture. Fit water IN and OUT in the condenser, must remember cool water should pass through below to top of condenser to avoid air bubbles. Then after fill n-Hexane or petroleum ether (40-60C) in siphon tube it would Frist siphon then fill half as well on siphon tube. Start heating on water bath The temperature of water bath should be 70- 75C. Run the system till 7 hours, for clearance n-hexane will clear at siphon tube, it means extraction is completed.

Then after remove the sample from siphon tube, recover n-hexane, Keep filter paper sample and flask in the drying oven for 3 hours. When the smell of sample is free from ether, it means it has been dried.Weigh filter paper & flask. Extracted oil will collect in flask.

The Soxhlet extraction process is the most useful technique for solid-liquid extraction in many fields like Agriculture, Pharmaceuticals, Foodstuffs, and also in the Environment.

1. Table No. 5: - Name of Apparatus Supplier.

Sr. No.	Name of Apparatus	Supplier
1	Beaker	Actria
2	Measuring cylinder	Borosil
3	Pipette	Borosil
4	Glass rod	Borosil
5	Petri dish	Borosil
6	Funnel	Omsons germany

Compatibility Studies

To ensure TDDS (Transdermal Drug Delivery System) components are compatible during preparation, it's crucial to assess their compatibility using various analytical and physical tests. These include evaluating the drug's solubility in the chosen polymer and plasticizer, assessing the adhesive properties of the pressure-sensitive adhesive, and ensuring the backing material is compatible with the other components and the drug. Furthermore, physical tests like drug content uniformity, thickness, and in vitro drug release studies help confirm the patch's integrity and performance.

1. Drug-Excipient Compatibility

Solubility- The drug needs to be soluble in the polymer and plasticizer used in the patch formulation. Incompatible combinations can lead to phase separation or precipitation, which can affect drug release and patch stability.

PVA is dissolved in water, then mixed with diclofenac (often from a methanol solution) No covalent reaction occurs between PVA and diclofenac.by including both in solution, need to **mixed solvent** (e.g., methanol + water) where:

- Water dissolves PVA,
- Methanol boosts diclofenac solubility.
- Drug and polymer also compatible with plasticezer (PG,glycerol)

Molecular Compatibility

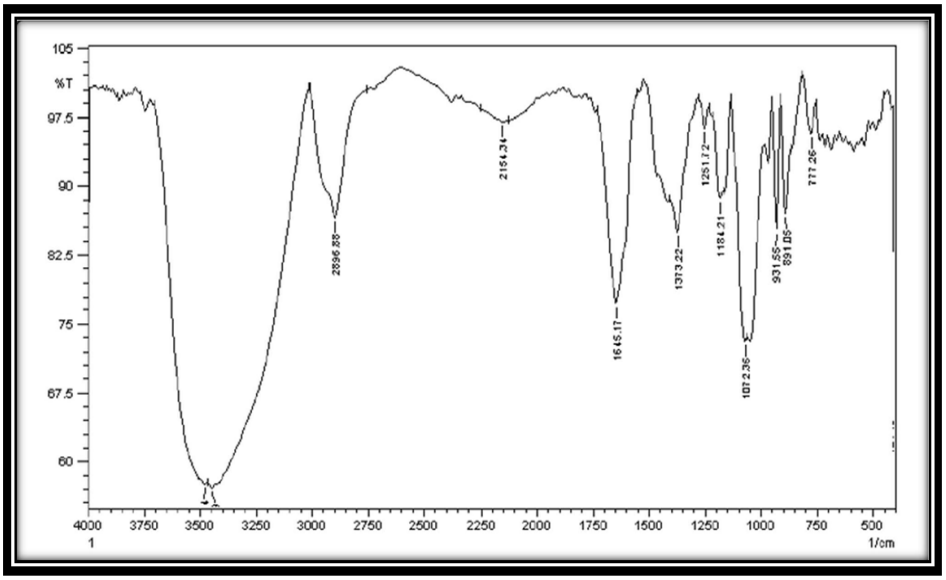
Techniques like differential scanning calorimetry (DSC) and Fourier transform infrared spectroscopy (FTIR) can be used to assess if there are any chemical interactions between the drug and excipients. Several studies using Fourier Transform Infrared (FTIR) spectroscopy show that when Diclofenac sodium is loaded into PVA (e.g., dual-layer patches), all characteristic peaks of the drug remain present without new bonds forming. This indicates that Diclofenac sodium remains intact, and there are no harmful chemical reactions between Diclofenac sodium and PVA—just favorable intermolecular interactions. In multi-layer PVA patches, the presence of distinct Diclofenac sodium peaks in FTIR spectra confirms chemical and structural compatibility.

Stable Physical Dispersion and Controlled Release

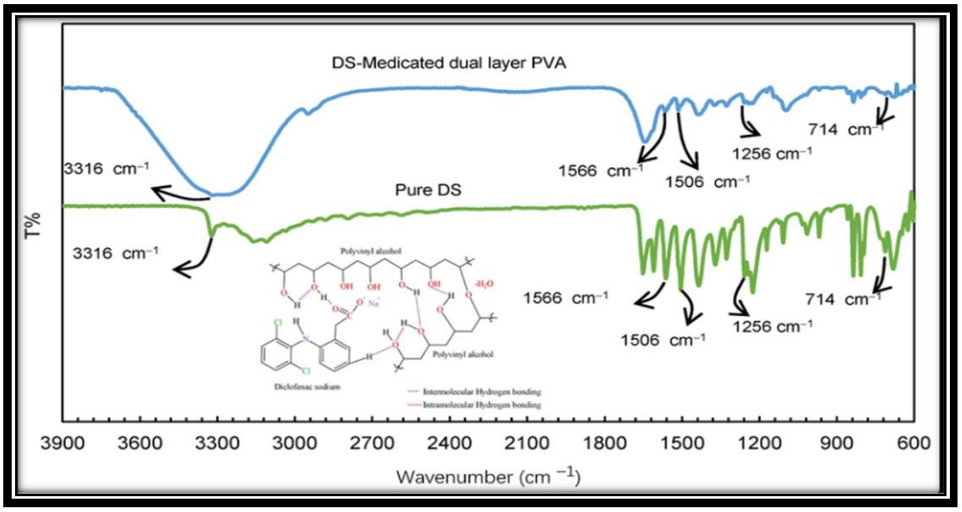
DS disperses uniformly within PVA hydrogels or patches, often becoming molecularly amorphous, which promotes stability and prevents crystallization.

Biocompatibility of PVA Excipient

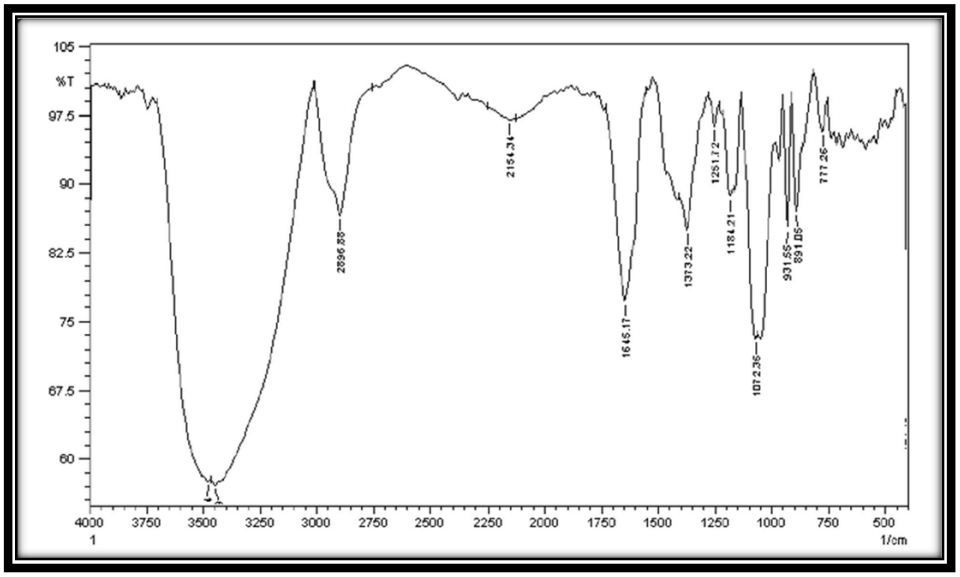
PVA is widely used in biomedical applications—contact lenses, hydrogels, and drug carriers— thanks to its non-toxic, hydrophilic, and chemically inert nature. When used with diclofenac sodium, PVA acts as a stable polymer matrix without undesirable reactions, ensuring pharmaceutical safety.



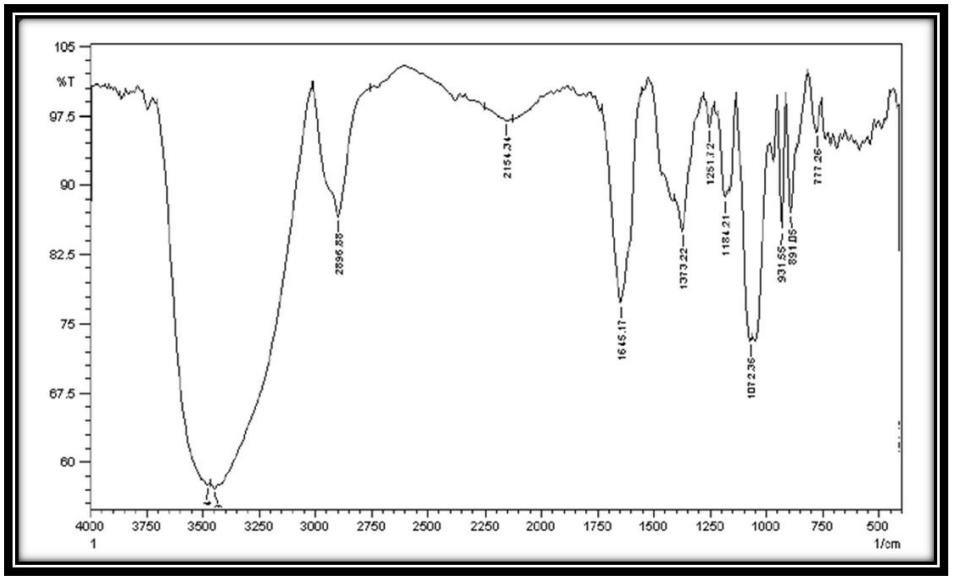
No.14: FTIR spectrum of pure Diclofenac sodium (API)



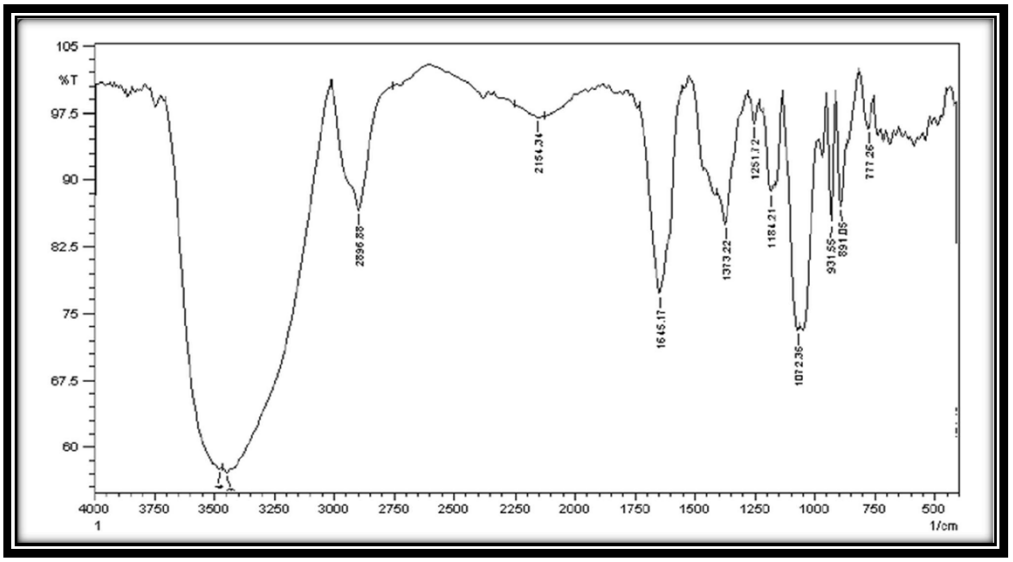
No.15: - FTIR spectrum of DS and PVA.



No.16: - FTIR spectrum of DS and Banana Extract.



No.17: - FTIR spectrum of DS and Okra Extract.



No.18: - FTIR spectrum of DS and DMSO.

Retention of DS characteristic peaks

A distinct N–H stretching peak at ~3316 cm^{-1} Carboxyl C=O stretching at ~1566 cm^{-1} Aromatic C=C stretching near 1506 cm^{-1}

C–N stretching around 1256 cm^{-1}

C–Cl vibrations between 650–780 cm^{-1} No evidence of new bonding

The FTIR spectra of DS-loaded PVA closely match pure DS and PVA reference spectra, with no new peaks—indicating physical mixing rather than chemical reaction, confirming molecular compatibility. The FTIR graph (above) illustrates that all characteristic DS bands are intact in the PVA patch, with no new peaks suggesting chemical interactions. This confirms **excellent physicochemical compatibility** between DS and PVA, as required for drug delivery systems.

DMSO and Diclofenac Sodium stability

Diclofenac sodium dissolves extraordinarily well in DMSO—studies find solubility over 100 mg/g, which is about 100×higher than in solvents like acetone or ethyl acetate. DMSO acts as **a polar aprotic solvent** that dissolves diclofenac and carries it across the skin. It does not chemically react with the drug—only enhances permeability.

Aspect Evidence

High solubility-~100–200 mg/mL in DMSO across various studies

Stable formulation-Used in FDA-approved **nonsteroidal anti-inflammatory drug** (NSAID) containing ~45% DMSO

No degradation-Physicochemical data show no adverse interactions—DMSO simply dissolves, no **new bonds.**

Solubility: Diclofenac dissolves extremely well in DMSO, enabling high-concentration stock/preparation

Formulation Use: DMSO-based gels/solutions with diclofenac are clinically established

Chemical Stability: No evidence of chemical degradation or interaction—just effective solvent behavior.

2. Adhesive Selection and Testing

Adhesive Properties: The chosen adhesive must provide adequate adhesion to the skin without causing irritation or allergic reactions, in the prepared patch, banana peel extract and okra extract are providing adhesive property to the patch Peel Adhesion: This test measures the force required to remove the adhesive from a substrate, ensuring it adheres well to the skin. Shear Adhesion: This test measures the ability of the adhesive to withstand stress and maintain adhesion under shear force, preventing the patch from detaching prematurely.

3. Physical Characterization

Drug Content Uniformity: This ensures that the drug is distributed evenly throughout the patch, guaranteeing consistent dosage delivery.

Thickness: The thickness of the patch affects the drug release rate and should be consistent.

In Vitro Drug Release Studies: These studies assess how the drug is released from the patch over time under simulated physiological conditions.

4. Membrane and Backing Material Compatibility

Membrane Permeability: The membrane controls the drug release rate and should be compatible with the drug and other components. The backing membrane used in the patch is compatible with all components.

Backing Material: This material protects the patch and should be impermeable to the drug and moisture.

5. Stability Studies

Long-term Stability: The patch needs to be stable under different storage conditions (temperature, humidity) to maintain its efficacy and safety.

6. Irritation and Sensitization Testing

Skin Irritation: The patch should not cause skin irritation or allergic reactions.

Sensitization: The patch should not induce sensitization (increased reactivity to the substance).

- **Standard calibration curve of diclofenac sodium**

Concentration of 0.5mg/ml was prepared by dissolving 50.2mg of diclofenac sodium in 100ml of Citro-phosphate buffer solution (pH 7.4). Following this; 2ml, 4ml, 6ml, 8ml, 10ml and 12ml of this solution were obtained and diluted to 100ml separately. 2ml aliquot, from each dilution, was then taken out for diluting to 20ml with citro-phosphate buffer solution (pH 7.2) and preparing the concentrations of 0.001, 0.002, 0.003, 0.004, 0.005, and 0.006 mg/ml. UV spectrophotometric analysis of these concentrations was performed at 276 nm wavelength Fig. 1 shows the recorded absorbance at the different prepared concentrations.

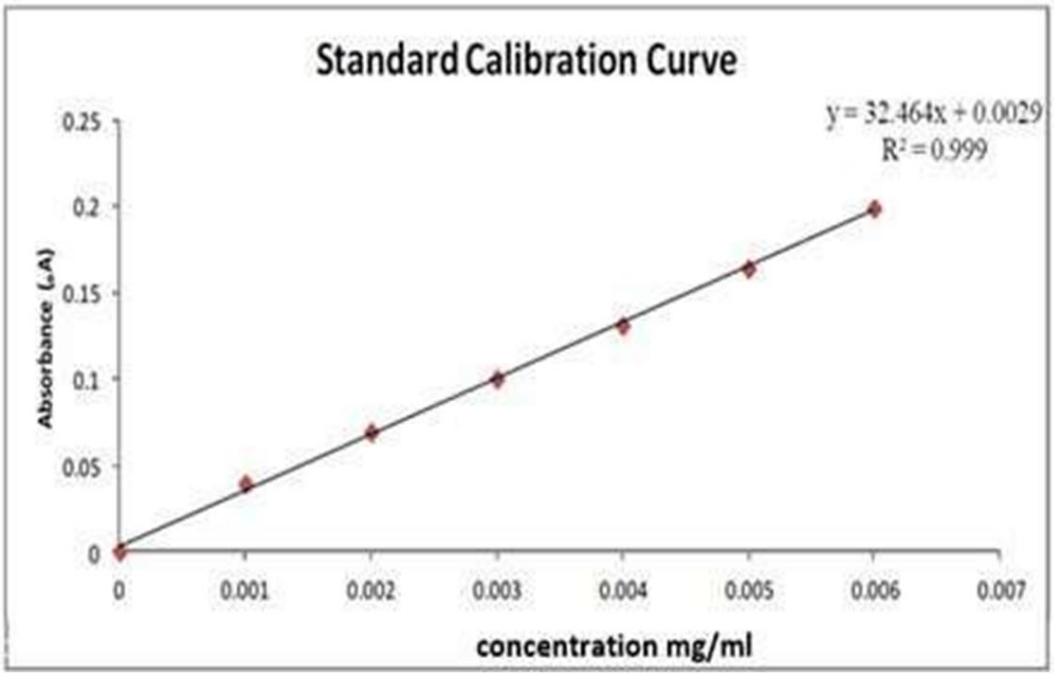


Fig No.19: - Standard calibration curve of diclofenac sodium.

Preparation of Medicated Patch

Films were prepared by the film casting method of specially designed glass melds with the plastic transparent sheet. Different combination of polymers like PVA: MC were used for preparation of films. Varying proportion of polymers in each pair was dissolved in solvents such as water and methanol ethanol, respectively. The final concentration of mixture of polymers in each solution was 10%. Solutions were prepared at room temperature using plasticizers as 30% propylene glycol for MC: PVA.

Drug was incorporated in 10% polymer solution, obtained by stirring on magnetic stirrer. Polymeric solution was poured within a glass bangle placed on glass mold. The rate of evaporation of solvent was controlled by inverting cup funnel. After 24 hours the dried films weretaken out and stored in desiccator.[11]

Evaluation of Medicated Patch: - 1 - Weight of Patch

Transdermal patches were weighed on analytical balance and average weight was determined for each film. It is desirable that films should have nearly constant weight. It is useful to ensure that a film contains the proper number of excipients and API.[11]

2 - Thicknesses of Patch

The thickness of the patch was measured by micrometer screw gauge at five different places; an average of three values was calculated. This is essential to ascertain uniformity in the thickness of the film this is directly related to the accuracy of dose in the film.[11]

3 - Surface pH

The film was put in glass tube containing 10ml DW, after one hour, the pH of film surface measured by using digital pH meter, this method done in triplicate.[24]

4 - Folding Endurance

Folding endurance done by reparative folding three randomly film at same point until break, the number of times of film folded at same point without rupture gave the number of folding endurance value.[25]

5 - Content Uniformity

Drug content was determined by dissolving the film containing 3 mg of drug in 100 ml phosphate buffer pH 7.4 to get 30µg/ml solutions. An aliquot of 1ml sample was withdrawn diluted to 10 ml with water. Then solution was filtered through Whatman filter paper and analyzed by UV- spectrophotometer at λ max of drug.

Content uniformity studies were carried out in triplicates for each batch of the film.[11]

6- In-Vitro Drug Release

Patches were firmly secured in beaker (100ml) placed on magnetic stirrer and 100 ml phosphate buffer saline (PBS pH 7.4) added as the dissolution medium. At specified times (1, 2, 3, 4, 5, 6, 7, 8 hours) 5ml aliquots were removed using a syringe and replaced with equal volumes of fresh PBS to maintain the total volume. Samples were filtered through Whatman filter paper and concentration of diclofenac determined by measuring absorbance at 276 nm.[11]

7 - Percentage moisture content

The prepared transdermal films were individually weighed and stored in a desiccator containing fused calcium chloride at room temperature for 24 h. After 24 h, the films were reweighed and the percentage moisture content was determined from the following formula. Percentage Moisture Content = Initial weight − Final weight Final weight x100.[19]

8 - Percentage moisture uptake

The prepared transdermal films were individually weighed and stored in a desiccator containing a fused saturated solution of potassium chloride to maintain 84% RH for 24 h at room temperature. After 24 h, the films were reweighed and the percentage moisture uptake was calculated using the following formula. Percentage Moisture Uptake = Final weight − Initial weight Initial weight x100.[19]

9 - Percentage elongation break test

The percentage elongation break was calculated by noting the length just before the breaking point and the following formula was used to calculate the percentage elongation. Percentage Elongation = Final length of strip − Initial length of strip intimal length of strip x100.[19]

7 - Thumb tack test

It is a qualitative test applied for tack property determination of the adhesive. The thumb simply pressed on the adhesive and the relative tack property is detected.[26]

Table No. 6: - Formula's Composition of Diclofenac Sodium Transdermal Film.

FORMULATION INGREDIENTS	FORMULATION CODES						
	F1	F2	F3	F4	F5	F6	F7
API	190mg	190 mg	190 mg	190 mg	190mg	190mg	190mg
POLYVINYL ALOCHOL	500mg	600mg	300mg	800mg	200mg	350mg	400mg
METHYL CELLULOSE	500mg	400mg	700mg	200mg	800mg	650mg	600mg
PROPYLENE GLYCOL	7 ml	3 ml	2 ml	4 ml	3ml	3.5ml	3ml
ETHANOL	q.s	q. s	q.s	q.s	q.s	q.s	q.s
WATER	q.s	q.s	q.s	q.s	q.s	q.s	q.s
GLYCEROL	q.s	q.s	q.s	q.s	q.s	0.5 ml	0.5ml
Banana Peel Extract	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Okra Extract	q.s	q.s	q.s	q.s	q.s	q.s	q.s
DMSO	q.s	q.s	q.s	q.s	q.s	q.s	q.ss

Evaluation Of Diclofenac Sodium Patch: - Evaluation parameter: -

Table No. 7: - Physical Evaluation Parameter Of Diclofenac Sodium Patch.

Formulation Codes	Average weight (Mg)	Thickness	PH	Folding endurance	% moisture content	% moisture uptake	Adhesive property	Appearance
F1	35±0.1	1±0.8 mm	7.1 ±1	135±5	25	-18	Good	Semi- Transparent, sticky
F2	40±0.1	1±0.7 mm	6.5± 1	138±5	22.1	-15	Good	Transparent, sticky
F3	45±0.1	1 ±0.5 mm	6.6± 1	141±4	24	-16	Good	Transparent
F4	39.2±0.1	1±0.6 mm	6.3 ±1	151±3	23	-12	Good	Transparent
F5	40.5±0.1	1 ±0.4 mm	6.5 ±1	155±2	22	-14	Good	Transparent
F6	37.2±0.1	1 ± 0.3mm	6.9 ±1	140±3	23.5	-16	Good	Transparent
F7	38.5±0.5	1± 0.2 mm	6.8 ±1	160±6	21	-06	Good	Semi- Transparent, sticky

Table No. 8: In Vitro Drug Release Test by UV Spectroscopic λ max(276nm) Of Batch F1.

Time (Min)	Absorbance (276nm)	% Drug release
5	0.478	50.30
15	0.581	63.51
30	0.582	63.52
45	0.678	75.10
60	0.687	76.30
90	0.688	83.20
120	0.751	84.21
140	0.851	92.97
Abs of Std. 0.912 = 100%		

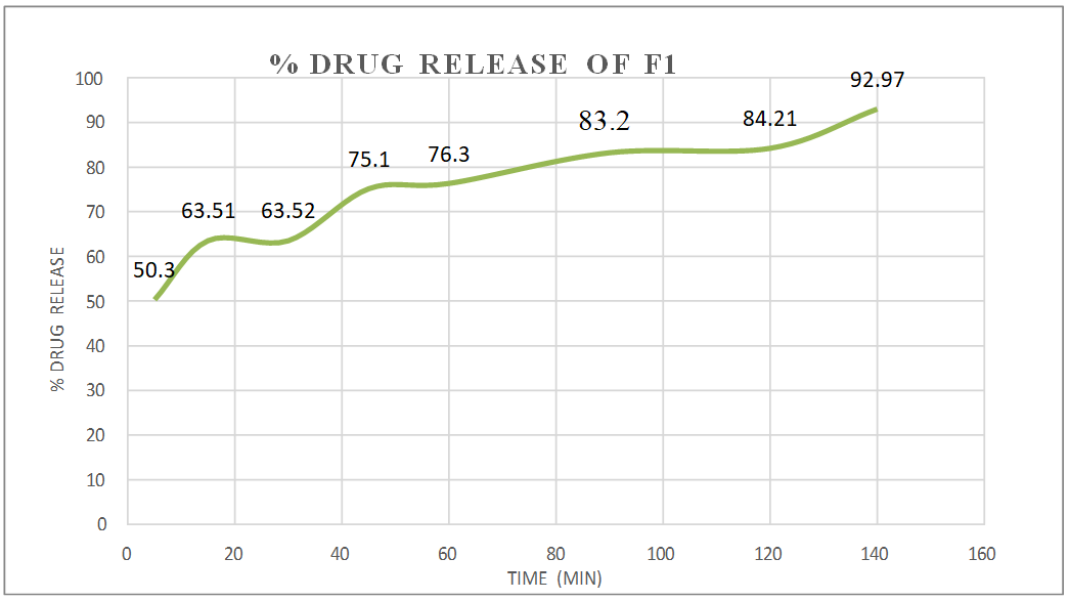


Fig. No. 20 Graph of In-vitro drug Release of` batch F1.

Time (Min)	Absorbance (276nm)	% Drug release
5	0.490	51.30
15	0.590	64.10
30	0.599	64.90
45	0.680	75.50
60	0.690	76.50
90	0.698	84.20
120	0.780	85.20
140	0.990	95.16
Abs of Std. 0.912 = 100%		

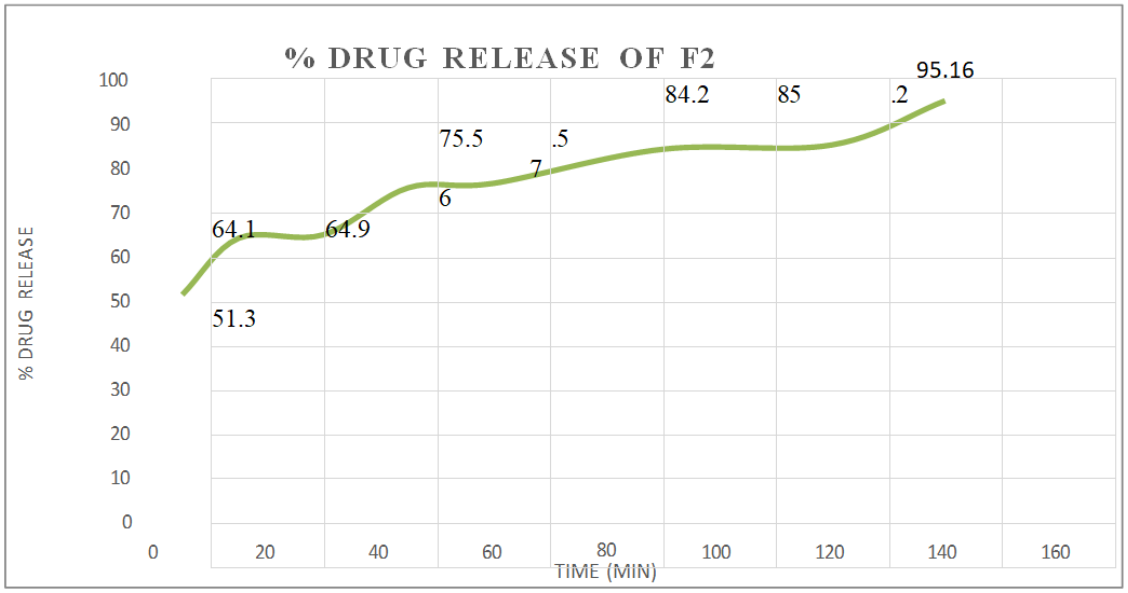


Fig. No. 21:- Graph of In-vitro drug Release of` batch F2.

Time (Min)	Absorbance (276nm)	% Drug release
5	0.499	60.10
15	0.595	64.60
30	0.600	64.69
45	0.685	75.60
60	0.695	76.55
90	0.699	84.30
120	0.785	85.30
140	0.895	95.22
Abs of Std. 0.912 = 100%		

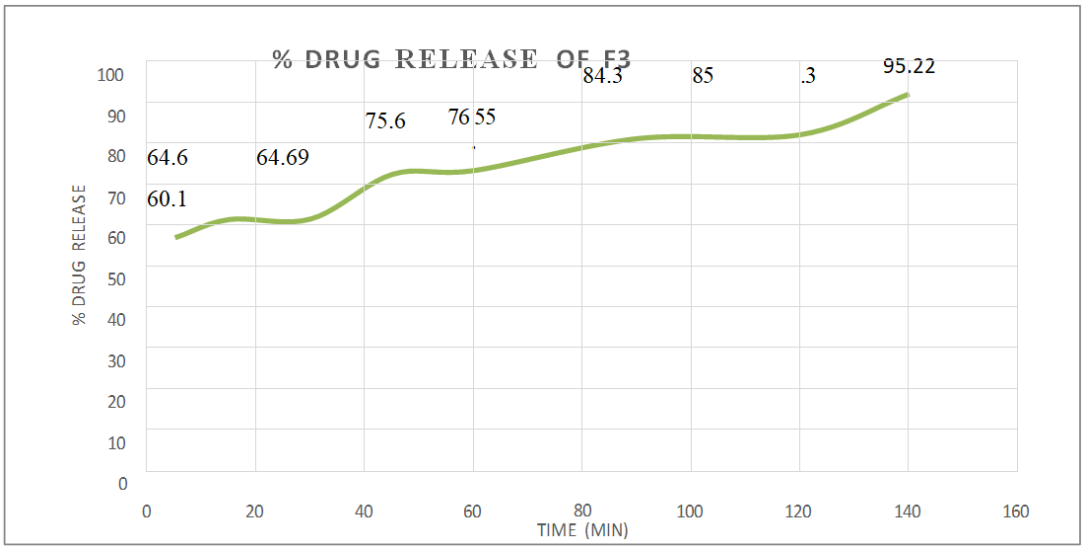


Fig. No.22:- Graph of In-vitro drug Release of`batch F3.

Table No. 11: In Vitro Drug Release Test by UV Spectroscopic λ max(276nm) Of Batch F4.

Time (Min)	Absorbance (276nm)	% Drug release
5	0.500	60.50
15	0.589	64.78
30	0.610	65.98
45	0.690	73.20
60	0.698	83.10

90	0.700	83.25
120	0.787	85.20
140	0.898	95.80
Abs of Std. 0.912 = 100%		

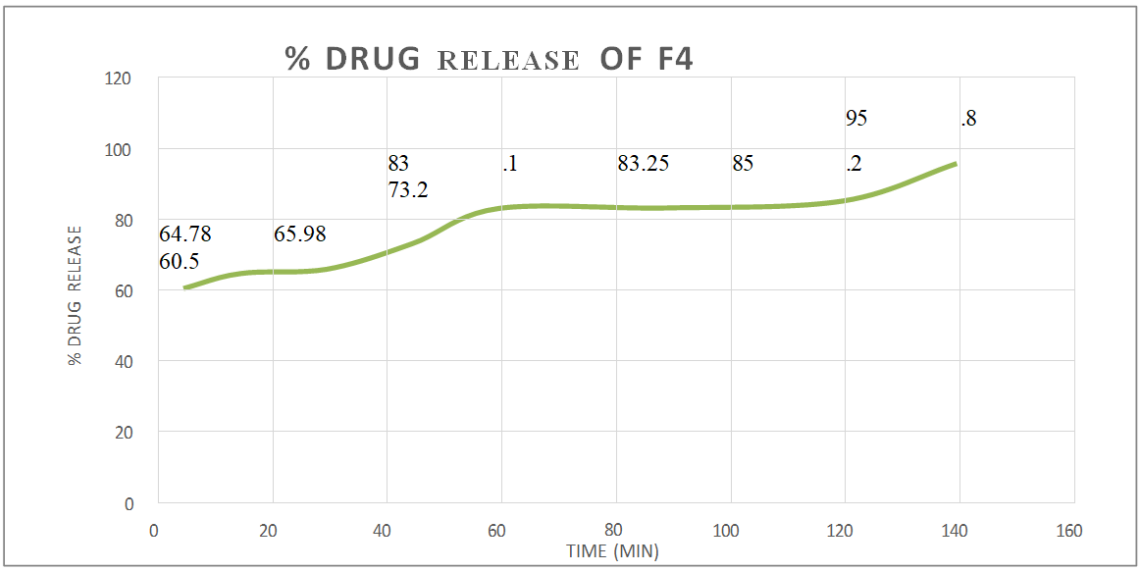


Fig. No.23:- Graph of In-vitro drug Release of` batch F4.

Table No. 12: In Vitro Drug Release Test by UV Spectroscopic λ max(276nm) Of Batch F5.

Time (Min)	Absorbance (276nm)	% Drug release
5	0.585	64.30
15	0.710	78.01
30	0.762	84.10
45	0.772	85.12
60	0.829	91.20
90	0.852	92.98
120	0.873	96.10
140	0.905	99.45
Abs of Std. 0.912 = 100%		

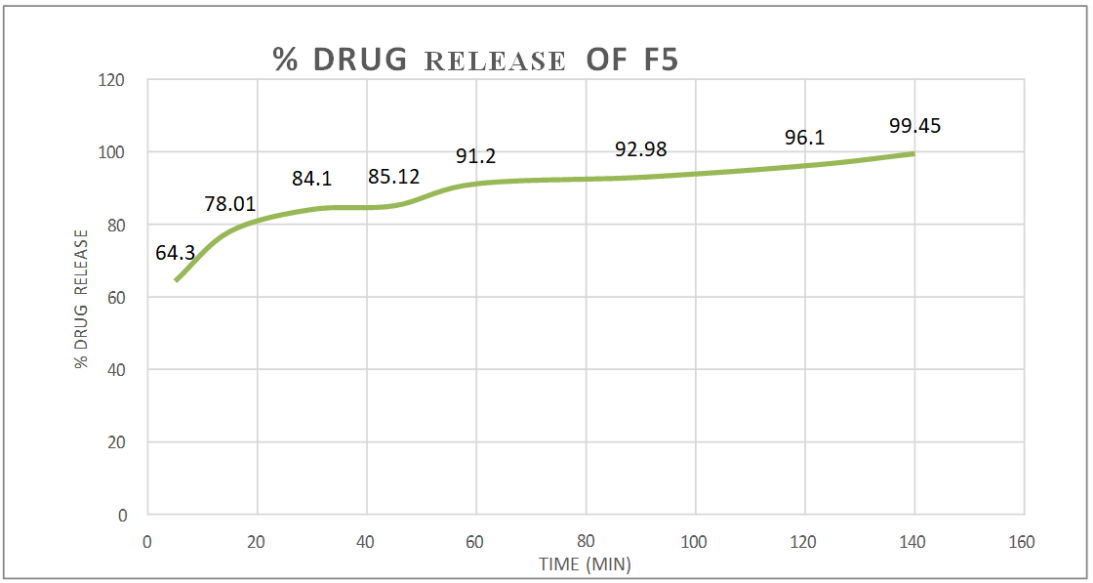


Fig. No. 24:- Graph of In-vitro drug Release of` batch F5.

Table No. 13: In Vitro Drug Release Test by UV Spectroscopic λ max(276nm) Of Batch F6.

Time (Min)	Absorbance (276nm)	% Drug release
5	0.588	64.56
15	0.718	79.02
30	0.765	84.18
45	0.775	85.29
60	0.830	91.30
90	0.856	93.94
120	0.874	96.14
140	0.908	99.85
Abs of Std. 0.912 = 100%		

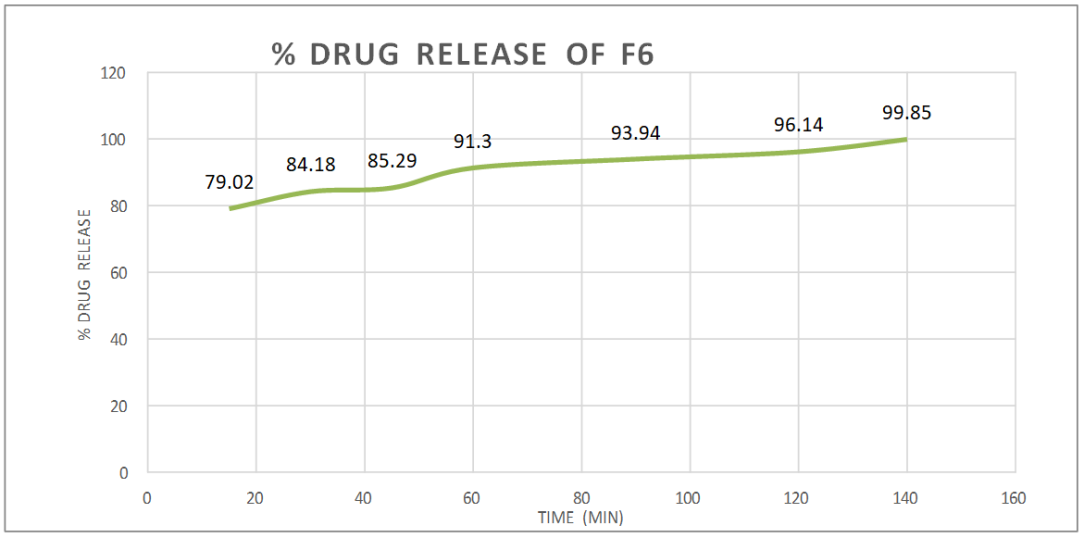


Fig. No.25:- Graph of In-vitro drug Release of` batch F6.

RESULT AND DISCUSSION

From the obtained results it was seen all the prepared film have weight uniformity which range from (**35±0.1-45±0.1** mg), all the formulas showed acceptable thickness (**1±0.2**mm) with folding endurance more than 160, which mean the prepared films flexible enough when handling and transport without broken. The surface pH ranges from (**6.3 -7.1**) gave indication there is no side effect or irritation to the skin.

Formulation F7 was found to possess other parameters at a significantly optimum level; that's why F7 formulation was selected for drug permeation study. Data obtained from drug permeation study for the formulation F7 is shown below in table 15.

❖ **Content Uniformity test: - λ max is (276 nm).**

Fig No.26: - Sample Content Uniformity.

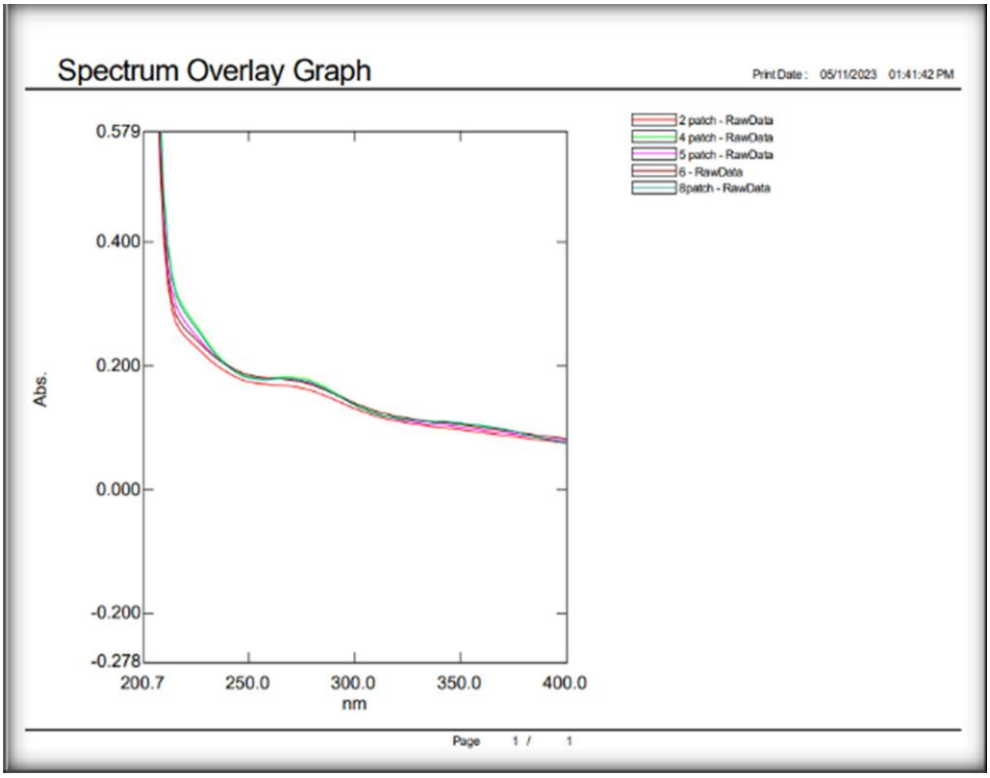


Fig. no.27: - Spectrum Overlay Graph.

Table No. 14: - Content uniformity.

PATCH NO.	ABSORBANCE
Patch1	**0.163 nm**
Patch2	**0.179 nm**
Patch3	**0.175 nm**
Patch4	**0.173 nm**
Patch5	**0.176 nm**
SD (σ)	**0.00609918**

Table No. 15: - In Vitro Drug Release Test by UV Spectroscopic λ max(276nm) Of Optimize Batch F7.

Time (Min)	Absorbance (276nm)	% Drug release
5	0.589	64.58
15	0.721	79.06
30	0.768	84.21
45	0.778	85.31
60	0.833	91.34
90	0.857	93.97
120	0.877	96.16
140	0.910	99.99
Abs of Std. 0.912 = 100%		

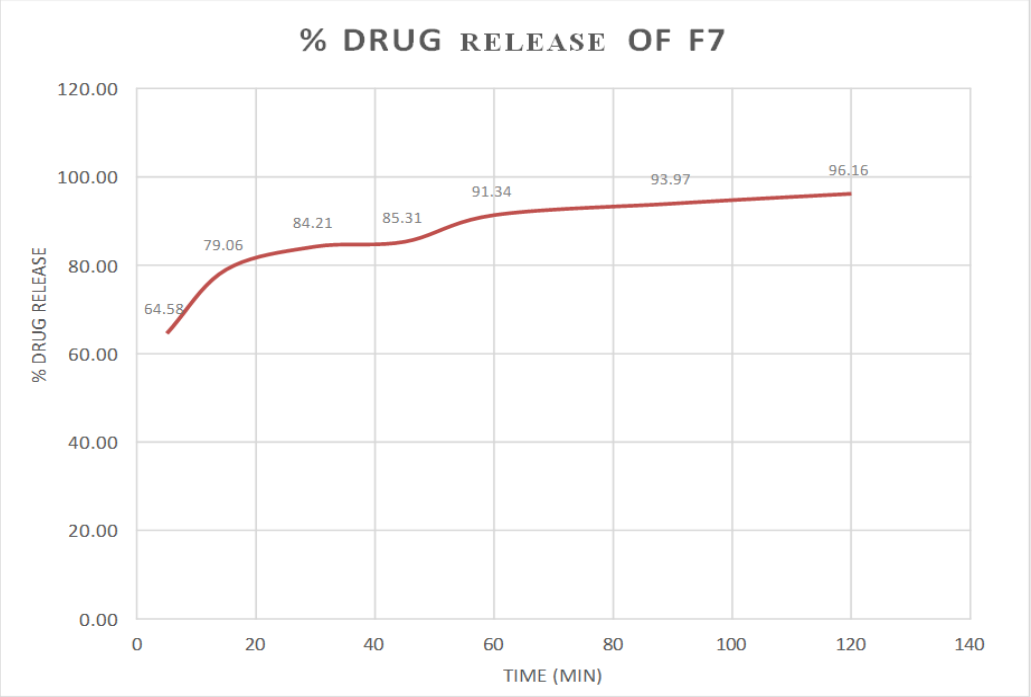


Fig. No.28:- Graph of In-vitro drug Release of` batch F7.

CONCLUSION

We have prepared Patch containing natural release retardant the method of Preparation is reproducible and stable Ground-breaking technology of Patch containing natural release retardant might work in the safe and controlled delivery of diclofenac for various headache Problem. It might work successfully by reducing the problems of migraine, Minor stains, sprains and improving patients' compliance. Further studies are recommended for the development transdermal patch containing a natural release retardant.

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