



## NOVEL APPROACHES AND FUTURE TRENDS IN DIFFERENT POLYHERBAL FORMULATIONS OF BUCCAL PATCHES

Yadav V.D.,<sup>1</sup> Gaikwad S.S.\*<sup>1</sup>, Babar A.S.<sup>1</sup>, Tarke Santosh.R.<sup>2</sup>, Mrunal K. Shirsat<sup>2</sup>

1. Department of Pharmaceutics, Arvind Gavali college of Pharmacy Jaitapur, Satara, Gat. No.261, At-Jaitapur, Post-Chinchner-vandan, Satara-415004, Maharashtra, India.

2. Department of Pharmacognosy, B.S.P. M's B. Pharmacy college, Modi learning center, Ring road Ambajogai, Beed, Maharashtra, India.

*Correspondence author: Ms. Gaikwad S.S.*  
[shivani.gaikwad2803@gmail.com](mailto:shivani.gaikwad2803@gmail.com)

### ABSTRACT

In this article, it should have tried to provide a glimpse of the future aspects and developing techniques in buccal drug delivery through patches with aid of herbal constituents. It contains information of how buccal delivery of drugs can be enhanced through the modifications in other drug delivery technologies and combining these to give superior delivery of drugs. Buccal patch is one of the novel dosage forms that have many advantages over other drug delivery systems. Other modification may be carried out to buccal patches in order to improve the efficacy. Some examples include buccal patches loaded with nanoparticles of chitosan containing insulin. Herbal constituents have wide range of advantages in patch delivery. Variety of modified drug technologies can be utilized in developing the buccal patch to improve the buccal drug delivery. e.g., Liposomes, niosomes, ethosomes, SLN, etc. These techniques can be merged together to form more efficacious and stable dosage form to improve overall drug delivery therapy.

**Keywords:** buccal patch, mucoadhesive, transmucosal delivery, polyherbal.

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### INTRODUCTION

The buccal route is being used for years to administer drugs such as some steroids that undergo first-pass effect. latest idea in this route has been generated and concerned with delivery of peptide-protein drugs as non-parenteral, produced by recent techniques in biotechnology. The buccal route has many benefits like excellent accessibility, patient compliance, reasonable patient acceptance and it avoids first-pass effect. In order to optimize drug delivery via the buccal cavity, the use of adhesive types of drug has been investigated. Herbal drugs are gaining attention nowadays as it non-toxic, does not have any side effects and shows action for prolonged period of time. So the delivery of the herbal drugs via novel drug delivery system i.e. mucoadhesive buccal patch, this topic will be considered in this review. <sup>[1]</sup> Buccal patches are made of two laminates. First, an impermeable backing sheet is cast with the adhesive polymer's aqueous solution before being cut into the desired oval form. Even when it is challenged by

fluids, the film that is placed to the oral mucosa can be kept in place for at least 12 hours.<sup>[2]</sup> Buccal drug delivery became an alternative to the traditional oral route of drug administration in order to address shortcomings including high first pass effect and product degradation in the challenging GIT environment. The mouth mucosa receives a lot of blood, which maximizes the value of the results provided by buccal medications. Salivary drug transference is caused by a gradient in concentration. Flexible and having good bio-adhesive qualities are essential for effective buccal medication administration. The drug is released in a pre-determined, predictable and controlled manner to bring out the required therapeutic response.<sup>[3]</sup> Numerous bioadhesive dosage forms, including films, tablets, patches, discs, gels, and ointments, have been developed in recent years for delivery of drug via the buccal route. As per the patient ease and flexibility, buccal films are favored over muco-adhesive disc and tablet. They also guarantee more precise drug dose and extended residence duration as compared to gels and ointments, sustaining SR drug action. Buccal films also lessen pain by enhancing the efficiency of medications and defending the surface of the wound.<sup>[4]</sup>

### **Types of Buccal Patches:**

(1) **Matrix type-** The hydrophilic or lipophilic polymer matrix and the medication are combined to create matrix-style buccal patches. By moulding medicated polymer, a therapeutic disc with a specific surface area is created

(2) **In reservoir type-** Instead of including an adhesive, the reservoir system has a cavity for the medicine and any additives. By fastening a water-resistant backing, drug loss is prevented. Manufacturing techniques of Buccal Patches: Following manufacturing techniques are used in making mucoadhesive buccal patches/films

- 1) **Solvent casting:** In this technique, the necessary number of mucoadhesive polymers is mixed with solvent, and the polymer swells following mixing. The determined amount of plasticizer was added to the polymer mix. and vortexed once more. The required amount of medication was liquefied in a tiny amount of solvent system, introduced into the polymer solution, and thoroughly mixed. Following the release of trapped air, the mixture is poured into a petri dish that has been cleaned. Until the assessment tests are run, the patches that have been developed are kept in a desiccator.
- 2) **Direct milling:** In this method, no solvents are used to create the patches. For motorized mixing of medicine and excipients without presence of any liq. solution, direct milling or kneading procedures are used. The resulting material is rolled to the necessary thickness. After that, the underlying material is laminated. Because there is no chance of remaining solvents or health problems are caused by solvents, the solvent-free technique is preferred.
- 3) **Hot melt extrusion:** In this technique, a mixture of pharmaceutical excipients is heated to a molten state and forced through an aperture to produce various shapes. Controlled release matrix SR tablets, pellets, granules, and oral fast disintegrating dosage forms have

all been made using hot melt extrusion. Immiscible components are extruded with the medication in solid dispersion extrusion before solid dispersions are created. Finally, dies are used to mould the solid dispersions into films.

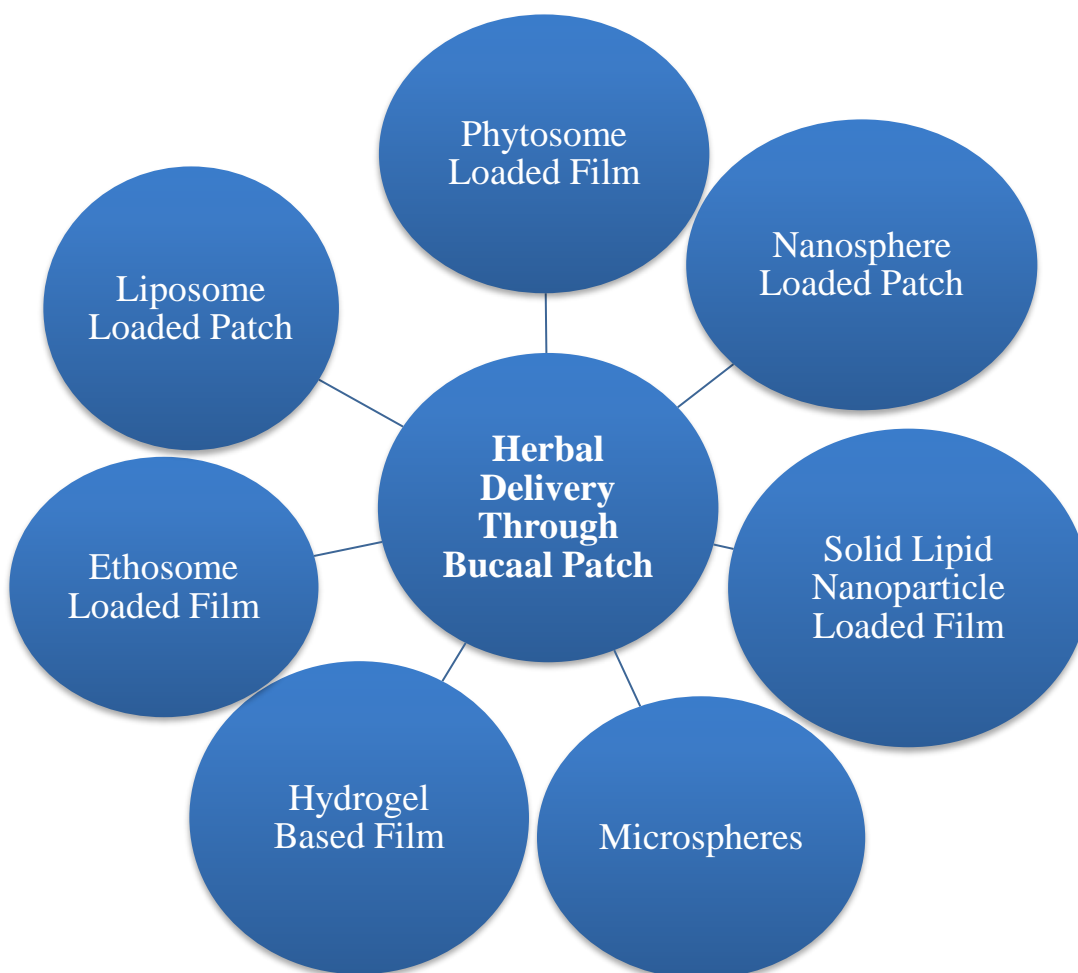
- 4) **Semisolid casting:** The semisolid casting technique begins by organizing solution of a water-soluble and film-forming polymer. An acid-insoluble polymer solution made with ammonium or sodium hydroxide is combined with the resulting solution. After adding the proper quantity of plasticizer, a gel mass is created. In the end, temperature-controlled drums are used to direct the gel-mass into the films.
- 5) **Rolling method:** This approach involves rolling a drug-containing solution or suspension on a carrier. Water and an alcohol-water mixture make up the majority of the solvent. The film is cut into the necessary shapes and sizes after being dried on rollers.<sup>[3]</sup>

### **Composition of buccal patches:**

- 1) **The active component.**
- 2) **Adhesive polymers:** HEC, HPC, PVP, PVA, carbopol, and other mucoadhesive polymers are examples of polymers in the adhesive layer.
- 3) **Diluents:** lactose, starch, and microcrystalline
- 4) **Sweeteners:** mannitol, sucralose, and aspartame.
- 5) **Flavoring substances:** menthol, vanilla, menthe oil, etc.
- 6) **Backing layer:** EC etc.
- 7) **Penetration enhancer:** Cyano-acrylate, etc.
- 8) **Plasticizers:** propylene glycol, PEG-100 and PEG-40, etc.<sup>[2]</sup>

Because of the powerful phyto-chemical components of certain plants are insufficient to produce the necessary therapeutic effect, the combination of diverse herbs, or polyherbs, in a specified ratio produces the needed therapeutic activity. The polyherbal formulation, which comprises two or more plants with various phyto-constituents and either alike or distinct therapeutic potential, has been effective in treating many illnesses. Because they have a broad therapeutic range, or because they are safe at high doses while still being efficacious at low doses, polyherbal formulations are quite popular. The seed, juice, root, gum, bark, stem, leaves, fruit, flower, and other portions of the plants are among the numerous components employed in Ayurvedic treatment. The goal of the current study was to develop and test a novel poly-herbal dispersible tablet containing aq. roots extracts of a few chosen plants with active phyto-constituents that have been scientifically shown to be effective in treating glomerulonephritis. These plants were chosen for the study under the following nomenclatures: *Angelica officinalis* (Umbelliferae), *Carica papaya* (Caricaceae), *Ficus hispida* (Moraceae), *Cassia fistula* (Fabaceae), *Boerhavia diffusa* (Nyctaginaceae), *Cichorium intybus* (Asteraceae), *Fumaria indica* (Fumariaceae materials and methods), *Crata* (Verbenaceae). On the root of the results of toxicity studies, the amount of medications employed in the formulation was evaluated based on drug tolerance studies and maximum effective dose. The equivalent quantity 25 mg of extract powder

has been used in this preparation for preparing poly-herbal dispersible tablet as active constituents. <sup>[4]</sup>



**Fig no.1: Scope for Novel Drug Delivery System Based Herbal Buccal Patch**

**Novel Drug Delivery System:**

**Targeting Drug System:** The term "targeting drug system" is another name for the targeted drug delivery system (TDDS). It is a novel medication delivery strategy with an improved therapeutic impact and fewer hazardous side effects that causes the pharmaceuticals to densely aggregate pathological-change structures. Three components make up a successful targeted medication delivery system:

- Controlled drug release;

- non-hazardous and biodegradable;
- Orientation cumulation;

In theory, the utilisation of biodegradable materials and microspheres and nanoparticles with high doses can effectively manage drug release half-life and degradation.

**Phytosome:** The distribution of important and effective herbal drugs has been demonstrated to be possible using phospholipid-based drug delivery systems. A new herbal medication delivery method called a "Phytosome" is created by complexing phosphatidyl choline and polyphenolic phytochemical constituents in the appropriate molar ratio. Conventional delivery system and innovative delivery system are connected via the phytolipids delivery system. The words "phyto" and "some," both of which refer to cell-like structures, are related in the term "phytosome," which also refers to a plant. Phytosomes are more effective herbal products than traditional herbal extracts since they are better absorbed and used to create greater effects. When compared to traditional herbal extracts, phytosomes exhibit superior pharmacokinetic and therapeutic characteristics. <sup>[5]</sup>**Liposomes:** A membranous lipid bi-layer made primarily of natural or manufactured phospholipids completely encloses the aqueous volume in liposomes, concentric bi-layered vesicles. The solvents are encapsulated inside the liposomes, which are spherical particles with free-floating solvents inside. Phospholipids, the building blocks of liposomes, are amphipathic molecules because they have a hydrophobic tail and a hydrophilic polar head.

Both hydrophilic and lipophilic substances can be contained within liposomes. The solubility, bioavailability, biodistribution, altered pharmacokinetics, and in vitro and in vivo stability of a component can all be improved by a liposome's unique features.<sup>[5]</sup>

**Nanoparticles** :Nanoparticles are small, sub-nanoscale structures made of artificial or partially artificial polymers. Nanoparticles of herbal medications have received a lot of attention recently. The size of the particles in nanoparticles, which range from 10 nm to 1000 nm, varies. Because the formulation may easily be encapsulated in it and go to the relevant spot, it is an effective system. The solid-core, spherical particles that are nanometric in size are known as nanospheres. The nanocapsules feature a vesicular system and contain medication that has been incorporated onto the surface or implanted in the matrix. Herbal extracts can be well protected against degradation, volatile losses, and early interaction with other substances by being microencapsulated in nanoparticulate.

**Microspheres:** Small, spherical particles called microspheres typically range in size from 1 μm to 1000 μm and have diameters in the micrometre range (1 μm). Micro-particles are another name for microspheres. Numerous organic and synthetic materials can be used to make microspheres. Commercially available microspheres include glass, polymer, and ceramic varieties. Microspheres can be categorised as biodegradable or not. Albumin and modified starch microspheres are examples of biodegradable microspheres.

**Ethosomes:**Ethosomes are elastic nanovesicles made of phospholipids with a high ethanol concentration (20–45%). It has been reported that ethanol is added to the vesicle system to produce the elastic nano-vesicles since it is an effective penetration enhancer. To enhance the distribution of different medications to the skin, ethosomes new lipid carriers made of ethanol,

phospho-lipids, and water ,were produced. Ethosomes are preferred for the transport of a variety of proteins and polypeptide compounds. For the comfort of the patient, ethosomes provide medication in the form of gel or cream. Solid lipid nanoparticles: It is a method that was created in 1990s. These are colloidal carrier designed specifically to carry chemicals that are lipophilic. It is prepared using a variety of techniques, including homogenization and heated micro-emulsion. Solid lipid nanoparticles range in size from 50 nm-1000 nm on average. Lipid matrix, the component of solid lipid nanoparticles, solidifies both at body temperature and at room temperature.

**Controlled Drug Delivery System:** The term "herbal GI controlled drug release dosage forms" refers to a new type of oral dosage form for administering a herbal extract as well as the method for doing so. In this dosage form, the herbal extract is coated on pellets, which are then either put inside of capsules or compressed into tablets. The aforementioned tablet is crushed from pellets that are coated with minimum two or more herbal extracts, and the aforementioned capsule might enclose pellets layered with one or more herbal extracts. Transdermal Drug Delivery System for Transdermal Drug Delivery (Transdermal Patches) The TDDS involves non-invasive transport the medication to the circulatory system from the skin's surface through its layers. A patch that is affixed to the bodily surface administers medication. A transdermal patch is an adhesive medical pad that is intended to deliver the active ingredient gradually over a number of hours to days after being applied to the skin. [5]

**Fig.No.2 Different Formulations of Herbal Constituents with Applications**

| TYPE OF FORMULATION | ACTIVE CONSTITUENTS | ACTIVITY   | APPLICATIONS                      |
|---------------------|---------------------|--|-----------------------------------|
| Liposomes           | Quercetin           | Antioxidant activity                               | Enhance therapeutic efficacy      |
|                     | Diospyrin           | Anti-cancer activity                               | Enhancement of anti-tumour effect |
|                     | Myrtus communis     | Antioxidant and antimicrobial activity             | Increase in its activities        |
| Phytosomes          | Oxymatrine          | Anti-viral   | Improvement of bioavailability    |
|                     | Ginkgo biloba       | Cardioprotective, anti asthmatic and anti diabetic | Induced hepatoprotective effect   |

|                           |                       |  |   |
|---------------------------|-----------------------|--|---|
|                           | Silybin               | Hepatoprotective and antioxidant<br>Increase in therapeutic effect | Increase in therapeutic effect  |
| Nanoparticles             | Hypocrellins          | Hypocrellins<br>Antiviral activity                                 | Improved performance in both stability and hydrophilicity             |
|                           | Ginseng               | Antioxidant activity   | enhancement in stability and in its action                            |
|                           | Quercitrin            | Antiinflammatory   | Better therapeutic for intestinal                                     |
| Solid Lipid Nanoparticles | Curcumin              | Antitumour, antioxidant and Antiinflammatory                       | Increase in stability   |
|                           | Curcuminoids          | antimalarial activity  | Increase in stability   |
| Emulsions                 | Rhubarb               | Cathartic and laxative activity                                    | Analysis of nine anthraquinones, bianthrones of rhubarb               |
|                           | Silybin               | Hepatoprotective   | Sustained release formulation   |
|                           | Matrine               | Antibacterial, Antiinflammatory, antiviral                         | Sustained release formulation   |
| Microspheres              | Ginsenoside           | Anticancer activity  | To enhance solubility and stability                                   |
|                           | Zedoary oil           | Hepato-protective  | Sustained release and high bioavailability                            |
|                           | Rutin                 | CVS and cerebrovascular diseases                                   | Targeting into cardiovascular and cerebrovascular regions             |
| Ethosomes                 | Sophora Alopécuroides | Anti-endotoxic, Anti-cancer & Anti-inflammatory                    | Ethosome enhances delivery of drugs through the stratum corneum layer |
|                           | Matrine               | Antibacterial, Antiinflammatory                                    | enhance the percutaneous permeation, improve anti-inflammatory effect |

The oral delivery method is the most agreeable among the delivery methods in terms of patient compliance. Many pharmaceutical companies have focused their research efforts on creating novel dosage formulations for previously prescribed medications. The oral strip, it is a thin film made up of hydrophilic polymers that quickly dissolves on the tongue or buccal mucosa, is one of these relatively recent dosage forms. The buccal mucosa is preferred above the sublingual mucosa in terms of systemic transmucosal medication distribution. One of the factors is that formulations meant for prolonged release action are more suited for the buccal mucosa, which is less permeable and therefore unable to cause a rapid commencement of absorption. Additionally, the buccal mucosa is more suitable for retentive systems utilised for oral transmucosal drug delivery since it is a generally immobile mucosa and is easily accessible. While direct patch formulation is possible, it can also be loaded with innovative particle systems to obtain more novel delivery and overcome challenges. Oral drug delivery research and development has resulted in the transformation of the dosage-forms from straightforward traditional tablets and capsules to the SR, CR or modified-release tablets and capsules, oral dispersible or disintegrating tablets (ODT), wafer, and most recently, oral strips (OS). The OS is essentially a postage stamp-sized, ultra-thin strip containing an active agent (API) along with various excipients. The benefits of easy dosing and mobility of OS have increased this dosage form's acceptance among both the pediatrics and geriatric populations. <sup>[6]</sup>

#### **Applications of Novel Nano-Structured Systems:**

Many herbal constituents have the potential for being effective in many diseases and disorders but main drawback of these constituent is low solubility. To overcome such drawback novel drug delivery system can be found of potential use to deliver these phytoconstituent.

Curcumin has been prepared in a variety of inventive formulations in an effort to increase its bioavailability. Promising innovative formulations include nanostructures, liposomes, micelles, and phospholipid complexes. These substances appear to have improved permeability, prolonged circulation, and resistance to metabolic pathways. Curcumin nanoparticles come in many different forms. These include curcumin loaded nanocrystals and conjugates, curcumin embedded polymer nanostructures, curcumin self-assemblies and nanogel, among others. The purpose of this topic is to describe the most recent developments in curcumin formulations that were made in an effort to increase curcumin's pharmacokinetics and/or bioavailability. Also highlighted are several intriguing ingredients employed in formulation development and the factors that improved their bioavailability. <sup>[7]</sup>To overcome significant barriers to curcumin's bioavailability, such as low solubility, instability and absorption, and rapid systemic metabolism, nano-formulation of the compound was created. Nanoparticles' (NPs) diameter and surface charge are significant. As is well knowledge, smaller particles have an advantage when passively targeting tumor tissue due to their increased permeability and retention effect. Additionally, larger zeta potentials have an impact on the stability of the particles as well as cellular absorption and intracellular trafficking. As a result, decreased renal excretion of curcumin and decreased liver metabolism could prolong the period that curcumin remains in the blood after being



delivered intravenously. Choosing the proper polymer composition, stabilizer, solvent, drug solubility, and preparation process are all important considerations when choosing a nanoparticle manufacturing method for the efficient encapsulation of active drugs. The composition of the materials utilized affects the size, polydispersity index, and entrapment effectiveness as well. [7]

To create formulations in the nano size range, herbal nanotechnology is being developed and used to polymeric systems (micro, nano). Nowadays, nanotechnology has developed into a versatile method of medication administration that is dependent on the dispersion of nanoparticles. When diluted in biological fluids, these nanoscaled delivery devices can instantly release the medicine in a free form. The compatibility of nanoscale with the architecture of medication administration at the cellular and subcellular levels is one of the few remaining types of applications. Herbal substances have gained a remarkable appreciation and acceptability as far as nano-technologies are concerned instead of filling a synthetic medication in a nano-carrier. Here, we've highlighted some of the drug delivery systems' covert properties, including those of phytosomes (a phytophospholipid complex), liposomes, the PEGylated-liposomes, the niosomes, NP, microspheres, and hydro-gels. [8]

**Hydrogels:** Due to their high water or moisture content and associated promise for diverse biotech and biomedical applications, hydrogels (HG) have attracted a lot of attention in recent years. Hydrogels are made of polymeric structures that are bind or simply hold together as water-swollen gels by one or more of the following interactions: primary covalent cross-links, hydrogen bonding, ionic forces, affinity or "bio-recognition" interactions, hydrophobic interactions, polymer crystallites, physical interferences of individual polymer chains, or combinations of two or more of the above interactions. These hydrogels are made by combining several diblock, triblock, or pentablock copolymers, which are then activated by environmental conditions such as temperature, pH, ions, etc. For the purpose of promoting wound healing, Xingyi Li et al. (2012) recently created a bio-degradable in-situ inj. nanocomposite hydrogel made of curcumin, N, O-carboxymethyl, chitosan, and oxidized alginate. The solubility of curcumin in water is  $\leq 0.1$  mg/ml, however following the formation of nano curcumin, it increased to 20 mg/ml. A consistent particle size of about 50 nm was achieved by lyophilizing this nano-curcumin into powder form. The hydrogel N,O-carboxy-methyl-chitosan-oxidized alginate (CCS-OA) was loaded with the prepared nano-curcumin. In PBS with a pH of 7.4, the hydrogel produced displayed a nice sustained release pattern. The release behavior of nano-curcumin from hydrogel is improved by the initial loading of the medication. In comparison to 2.5 mg of curcumin, the release rate of the 5 mg of curcumin loaded in CCS-OA hydrogel was slower i.e. 6.5%/day. [8]

## NOVEL FORMULATIONS

Transdermal patches and gels

## HERBAL CONSTITUENT

Guarana extract and khellin

|  |   |
|--|---|
| <b>Microemulsions</b>                        | Triptolide, babchi oil (psoralen)   |
| <b>SLN- Solid lipid nanoparticles</b>        | Camptothecin, triptolide, podophyllotoxin, curcumin, tetrandrine                            |
| <b>Polymeric conjugations</b>                | Camptothecin and podophyllotoxin  |
| <b>Scaffolds</b>                             | Tetrandrine   |
| <b>Nanoparticles &amp; micro-particles</b>   | Catechins, cuscuta chinensis, camptothecin, curcumin, hypericin, triptolide and tetrandrine |
| <b>Solid-dispersion &amp; matrix tablets</b> | Silymarin   |
| <b>Polymeric cardiac-stents</b>              | Curcumin  |
| <b>Liposomes and pro-liposomes</b>           | Catechins, calprotectin, curcumin, silymarin, and vincristine                               |

**Fig.No.3List of Novel Formulations and Herbal Constituents**

**Research Identified on Novel Formulations Containing Herbal Constituents:**In a study published by Rimjhim Sahu et, al., extracts of five specific herbs Glycyrrhiza glabra, Acacia-catechu, Punica-granatum, Curcuma-longa, and Mentha-piperita were combined to create a mucoadhesive gel for the treatment of oral aphthous ulcers of any cause. The gel was created at M/s Pharmanza Herbals Pvt. Ltd. in India using the Schmolka cold process. Active pharmaceutical ingredient (API) extracts in five different concentrations were used to create the formulations.<sup>[9]</sup>Mucin, a glycoprotein with a high concentration of negative charges that interact with chitosan's positive charges, is the primary component of mucus. Previous research has shown that the chitosan's physical and chemical properties promote an improvement of its mucoadhesive capabilities.<sup>[10, 19]</sup>Similar to chitosan in terms of biodegradation, low immunogenicity, mucoadhesiveness, and non-toxicity is sodium alginate, an anionic polymer. Due to the former's ability to increase absorption, mucoadhesive polysaccharides like chitosan and alginate are known to enhance the penetration of protein medicines through the intestinal mucosa. For the oral delivery of insulin, a range of alginate carriers, including beads, micro, and nanoparticles, have been researched for sustained release while guarding the medication against enzymatic destruction. <sup>[10]</sup>In a study by Neda Bavarsad et al., chitosan films were made by incorporating liposomes loaded with griseofulvin for topical medication delivery in superficial fungal infections. The films' mechanical characteristics, swelling, vapour transmission capability, drug release, temperature behaviour, and antifungal effectiveness against *Microsporungypseum* and *Epidermophyton floccosum* were all described. <sup>[11]</sup>A study was conducted by Zahra MahdizadehBarzoki et al. on the development of mucous adhesive buccal film/patches containing insulin as nanoparticles made of chitosan-gelatin bilayer. For the patch, Zahra MahdizadehBarzoki employed natural polymers like gelatin and chitosan. Chitosan is one of the

most popular natural polymers with mucoadhesive qualities. There are numerous different natural polymers. Chitosan has been used in numerous inventive compositions. The most prevalent biopolymer found in nature, chitosan has been utilised to prepare films and provide flexibility and rigidity. One of the hydrolyzed forms of collagen (a biopolymer) and animal proteins is gelatin. It provides the film its flexibility. The patch's formulation, which was improved using the CCD approach, has acceptable swelling and tensile characteristics. They are necessary conditions for a perfect buccal delivery mechanism. These two biodegradable polymers demonstrated good compatibility according to FTIR results.<sup>[12]</sup> Mucoadhesive Films Containing Chitosan-Coated Nanoparticles for Buccal Curcumin Release was the work of Let'icia Mazzarino et al. Turmeric contains a natural polyphenol component called curcumin, which has been proven to have a number of pharmacological properties. These properties include antioxidant, anti-inflammatory, antiviral, antibacterial, and anticancer properties. A mucoadhesive chitosan matrix containing nanoparticles coated with curcumin and loaded with chitosan was used to create nanostructured films. To create homogeneous and flexible films, several ratios of the mucoadhesive polysaccharide chitosan and a plasticizer agent were explored. The weight, thickness, shape, swelling, and in vitro curcumin release characteristics of the nanostructured films were assessed. The produced films' key benefit was that they contained nanoparticles that can transport the loaded medicine in a regulated manner and directly to the application location for extended periods of time. Additionally, because chitosan has the capacity to increase the penetration of molecules across the mucosal surface, using it to produce films and coat nanoparticles may increase the bioavailability of drugs. <sup>[13]</sup> It was the goal of Tarak A. Ahmed et al. to create an improved ethosomes preparation of glimepiride before loading it into the transdermal patches to provide a lower risk of medication side effects, a prolonged release pattern, and to prevent the first pass effect. Ethosomes are the lipid-based vesicular-particles with a high concentration of ethanol and water. Due to their distinctive characteristics and advantages, these particles have emerged. High drug entrapment effectiveness, high deformability, and improved transdermal penetration rate are characteristics of the drug delivery system. Transdermal films containing an ethosomal drug formulation demonstrated a prolonged drug-release manner and a lower maxi. drug conc. in the plasma of human volunteers, both of which will result in a decrease in the drug's negative effects. Finally, this drug delivery system could avoid the hepatic metabolism and considered a substitute administration route for acid-sensitive drugs. <sup>[14]</sup> Prudence Yedurkaret, al, to increase the bioavailability and therapeutic effectiveness of carvedilol, a multiple-unit system made up of muco-adhesive bilayer buccal tablets containing carvedilol-loaded with chitosan microspheres (CMs) were created. Spray drying was used to create drug-loaded CMs, which were then tested for their powder and particle characteristics before being crushed into bilayer buccal tablets with Carbopol. A. Placebo formulation (without the drug) and several bilayered- buccal tablet formulations with various ratios of the carvedilol-loaded CMs were created and tested for various characteristics. This study unequivocally proves the efficacy of bilayer- buccal tablets of carvedilol-loaded CMs in the management of hypertension since they are expected to satisfy patient compliance needs, manufacturing

requirements, and therapeutic requirements.<sup>[15]</sup>B. Al-Dhublab have prepared a zolpidem-loaded film of nanosphere. The polymer-matrix of the nanospheres, poly-lactic-co-glycolic acid (PLGA), was distributed in a layer of hydroxyl-propyl-methyl-cellulose (HPMC), eudragit LR 100, and carbopol 974 P. Ex vivo studies were carried out in Franz diffusion cells at 37.2 °C utilizing buccal mucosa of rabbit and synthetic saliva as the receptor medium. The film containing the 7.5% of Eudragit LR 100 had the maximum flow (93.8717.43 g/cm<sup>2</sup> /h), as compared to film containing 10% Eudragit LR 100 (75.3912.53 g/cm<sup>2</sup> /h). This could be a promising alternative drug delivery strategy that uses a buccoadhesive membrane covered with zolpidem nanospheres and gives a sustained release from poly (lactic-co-glycolic acid) [PLGA] nanospheres while yet having a rapid onset of action. <sup>[16]</sup>Elsabe' Jones and others the purpose of this research was to create and assess innovative nano-enabled films for DDI buccal administration. Before being included into monolayered multipolymeric films with nanotechnology enabled, SLNs were created by heat-aided homogenization and after ultra-sonication. Then its evaluation (MMFs). This study is significant because it established that employing SLNs to administer the drug (DDI) through the buccal-mucosa did not negatively impact the flux and it established the feasibility of administering DDI through the buccal method using nano-enabled MMF. The study's data showed for the first-time the capability of DDI-SLN prep. and nano enabled polymeric buccal films of SLN, to function as delivery platforms. <sup>[17]</sup>Malay K. Das et al. have researched rutin, one of the most popular flavonoids (*Ruta graveolens*) Rutin is used to treat capillary fragility, hypertension, UV radiation-induced cutaneous oxidative stress, hepatic and blood cholesterol, cataract, and cardiovascular disease. It also exhibits antioxidant, anti-inflammatory, antithrombotic, antineoplastic, and antiplatelet effects. The impenetrable stratum corneum was shown to be more permeable to Rutin phytosomes than to its free form. Skin uptake of Rutin phytosomes was 33.0 ± 1.33%, compared to 13.0 ± 87% for Rutin.<sup>[18-39]</sup>

## **CONCLUSION**

This article shows that there are number of delivery system and ways to improve the trans-mucosal delivery. Various novel dosage forms can be incorporated to form buccal patch with additional advantages. Incorporation of herbal constituents in the patch formulation promises an effective and non-toxic delivery of drugs. In this article we have tried to provide the data showing suitable ways to incorporate and use novel techniques, novel dosage forms along with the herbal components to create an improved drug delivery system.

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