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Review on Nanoparticle Loaded Oral Film an Innovative Approach for Poorly Water-Soluble Drug Delivery

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ABSTRACT: In this review Nanoparticle loaded oral film have been employed in this method of oral drug delivery to maximize therapeutic benefits while reducing toxic and unfavorable medication effects because enhances the pharmacokinetic and pharmacodynamics characteristics of (BCS) II and IV APIs capable of achieving targeted delivery and easy to provide oral drug delivery of API for high patient compliance for pediatric, geriatric, bedridden patients. More than 50% of APIs are having difficulty in the preparation of oral dosage form due to their poor oral bioavailability and aqueous solubility, primarily APIs in the Biopharmaceutical Classification System (BCS) II and IV. Therefore, API incorporated in Nanoparticles which have high drug carrier capacity, high stability and increase permeability as well as solubility in body fluid. The Nano encapsulated API loading in oral film is challenging occurs in formulation it overcome by selecting better film forming agent. Oral films are effective than oral fast-disintegrating tablets (OFDTs) to overcome the chocking problem for dysphagia and it provide, rapid onset of action, safety and efficacy, excellent dissolution profile.

Keywords: Nanoparticle, Nanoparticle Preparation, oral film, Method of Preparation, Composition of oral film.

INTRODUCTION

The present pharmaceutical delivery system contains over 90% of drugs, the majority of which have low water solubility. In a similar way, 60% of drugs now being studied fall under Biopharmaceutical Classification System (BCS) Class II &IV, where the bioavailability is constrained by the rate of dissolution. New therapeutic compounds with these features of limited solubility were discovered in recent developments in combinatorial chemistry. Since water makes up around 60% of the human body, low aqueous solubility makes it extremely difficult to administer these drugs (Müller *et al.*, 2001). If an active pharmaceutical ingredient (API), or medicine, is not dissolved in the gastrointestinal (GI) tract and is finally expelled, it cannot reach its receptor site in the body. Drugs that do not disintegrate simply cannot be therapeutic value (Niwa *et al.,* 2011).

Many techniques have been created to increase drug solubility or dissolution rate. These include:

(a) Particle Size Reduction (Bhakay *et al.,* 2014; Merisko-Liversidge *et al*., 2003)

(b) Crystal Engineering (Khadka *et al*., 2014; Zhang *et al.,* 2018).

(c) Micellar Solubilization (Vueba *et al.*, 2004).

(d) Inclusion Complex Formation (Liu *et al.*, 2017; Jansook *et al.*, 2010).

Since oral films have a larger surface area, which promotes rapid disintegration and dissolution in the oral cavity and increases bioavailability, they have a great deal of potential for the delivery of poorly soluble drugs. Although publications and patents show increasing interest in oral films for drug delivery, further studies are still needed, particularly for applications involving improving the bioavailability of poorly water-soluble drugs (Maher *et al.*, 2016).

The main focus of research and development in the area of water-insoluble drugs incorporated in oral films (Tomut *et al*., 2022). Unlike water-soluble drugs, which can be found in a dissolved condition or as a solid solution, water-insoluble drugs must be uniformly dispersed throughout a film in order to have a drug content that is acceptable. Recent patents outline a method for creating films with a consistent component distribution. These included no mention of the problems associated with employing micro particles or nanoparticles, or the inclusion of poorly soluble particles into films. Variations in the film's characteristics could also result from interactions between the drug's molecule and the polymer to incorporate poorly water-soluble drug Nanoparticle into films given that oral film has been shown to be a promising dosage form for drug delivery and Nanoparticle allow for dissolution and bioavailability enhancement for poorly water-soluble drugs (Chavan *et al.,* 2020).

Drug-loaded nanoparticles disperse in the oral film have certain advantages over the normal film like a higher rate of absorption in mucosal membrane and higher mucoadhesive properties. these nanoparticles were characterized in terms of size, charge, morphology, drug loading and drug release. Their properties are optimized in term of weight, thickness, folding endurance, surface pH, and muco-adhesian (Shen *et al*., 2013).

The oral film has been characterized by SEM, XRD, Raman spectroscopy and NIR chemical imaging analysis (Irfan *et al*., 2016). The SEM images showed that particles drugs were uniform dispersed in the films that had good drug content uniformity detected by NIR chemical imaging. XRD and Raman spectroscopy were to investigate the crystal structure of the APIs in the film.

Advantages:

1) They are improved oral bioavailability of poorly soluble drugs.
2) Taste masking of bitter drug is possible by taste masking technique (Zhu *et al.,* 2018)
3) No need of water.
4) No risk of chocking.
5) That avoid first pass metabolism by oral mucosal absorption.
6) It enhanced the stability of formulation.

Ideal Properties of Oral Film:

1) It should have an acceptable taste.
2) Pleasant mouth feels.
3) It should be less friable and have good mechanical strength.
4) It should have stable in environmental conditions.
5) On oral administration, it should not leave residue in mouth (Hannan *et al.*, 2016).
6) Film quickly dissolve to release a drug in the mouth.

Benefits of nanoparticle loaded in the oral film:

1) Nanoparticles have high drug carrier capacity, high stability and flexibility of incorporating biodegradable drugs, and accessibility to various routes of administration (Al-Nemrawi and Dave 2016).
1) The Film contain nanoparticle can be biodegradable, biocompatible and improved stability of film.
2) This nanoparticle-loaded oral film may be control release of drug and allow higher absorption of drug.
3) Film loaded nanoparticles shows higher mucoadhesive properties.

Limitations:

1) Highly potent drug molecule requires for loading.
2) The drug to be incorporated should have less dose up to 40 mg.
3) Drug should have a pleasant taste for patient compliance (Lopez *et al*., 2015).
4) Drugs with low and moderate molecular weight are prefer.
5) Good solubility in water as well as in saliva and also good stability.

Classification of Oral film(Panda *et al.,* 2012)**:**

There are three types of oral film as above:

1) Flash release
2) Mucoadhesive melt away wafer
3) Mucoadhesive sustained release wafer

List of different excipients used in the formulation of NPs along with their functions

1. Stabilizers. To stabilize the Nano emulsion prepared during particle preparation, a stabilizer is added to the formulation. But these stabilizers can also affect the characteristics of the obtained particles. The particle size may vary depending on the stabilizer's type and concentration (Wang *et al.,* 2017). The stabilizer, which is present at the interface between the organic and water phases during particle formation, can also be integrated on the surface of the particle, changing aspects like muco-adhesian and particle zeta potential. Size and zeta potential value are crucial physicochemical particle characteristics because they affect the preparation's physical stability and biopharmaceutical qualities (Lara *et al.*, 2013).

2. Co-surfactants. The co-surfactant will be an amphiphilic molecule and hydrophilic component which contain aromatic ring structure with lipophilic tail as a hydrophobic part, or a solid structure does not increase the mobility of the crystallized lipid at the interface. The stabilization of the Nano emulsion droplets during homogenization and during the polymorphic transition during storage was something we anticipated would be aided by an efficient co-surfactant (Date and Patravale 2004). The following are different co-surfactants high and low-melting lecithin's, non-ionic Tween 60 and 80, non-ionic polyoxyethylene, polyoxypropylene, polyoxyethylene block co-polymer Pluronic F68, and bile salt i.e. taurodeoxycholate (Araujo *et al*., 2009).

3. Organic solvent. When selecting an organic solvent to formulate nanoparticles, factors including the solvent's physical characteristics and capacity to dissolve drugs and polymers should be taken into account (Deshmukh and Niederberger 2017). An organic solvent can directly affect the particle size and entrapment efficacy, which in turn can influence the overall performance of the formulation, depending on its physical characteristics and capacity to dissolve the polymer and drugs.

Examples. Methanol, ethanol, chloroform, isopropanol, ethyl acetate, butyl lactatepropylene carbonate

4. Other additives. According to the requirement of the route of administration and the active agent properties additives are use like

(i) **Buffers.** Buffer's function is to stabilized the formulations by controlling the resulting pH change. However, if the chemicals in the buffer start interacting with the environment, they could cause either positive or negative changes to the system.

(ii) **Polyols.** The polyol uses a polyalcohol that functions as both a solvent and a moderate reducing agent, making it the ideal medium for the reduction of metal salt precursors (Carroll *et al*., 2011).

(iii) **Osmogenes.** Osmogene was used in a double emulsion (W/O/W)-solvent evaporation process to produce porous nanoparticles in Nano emulsion.

(iv) **Cryoprotectant.** Cryoprotectants must be utilized to eliminate extra moisture, improve long-term storage,

and safeguard the size stability of the CS-NPs during the freeze-drying process (Lee *et al*., 2009).

Techniques for Preparation of NPs

A. Solvent Evaporation. In solvent evaporation method, polymer is dissolved in a suitable organic solvent, such as dichloromethane, ethyl acetate, or ethyl acetate chloroform. The drug is dissolved in above mixture. Then, using mechanical stirring, sonication, or micro fluidization, the mixture of the polymer and drug solution was emulsified in an aqueous phase containing surfactant or emulsifying agent such as polysorbates, poloxamer, sodium dodecyl sulphates, poloxamer, polyvinyl alcohol, or gelatin to prepare an oil-in-water (o/w) type of emulsion in high-pressure homogenization through narrow channels (Pandey *et al*., 2016). When stirring continuously, the added organic solvent is evaporating after lypholization the formation of the emulsion due to the increasing temperature and decreased pressure. The type and amounts of stabilizer in this can have an impact on the particle size

B. Solvent Diffusion. This is a redesigned version for the solvent evaporation procedure. In this case, the polymer is dissolved in an aqueous solution which contains stabilizing agents. With the help of water miscible solvents like propylene, benzyl alcohol, etc., the polymer is dissolved in this way. The above solvent diffuses to the exterior phase and results the formation of Nano spheres or Nano capsules based on the ratio of oil to polymer. Interfacial turbulence causes tiny particles to develop between two phases as a result of the spontaneous diffusion of solvents. The reduction in particle size may be accomplished while the miscible solvent content may increase (Pragati *et al*., 2009). Both the solvent evaporation procedure and the solvent diffusion process can use hydrophilic or hydrophobic drugs. A multiple emulsion w/o/w must be formed when a hydrophilic drug is dissolved in the internal aqueous phase (Calderó *et al*., 2020).

C. Solvent Displacement or Nanoprecipitation Method. This technique was first described by Fessi *et al.* (1989). In that method involves precipitation of a preformed polymer from an organic phase, and with the presence or absence of a surface-active agent, the organic phase diffuses into the aqueous phase. Then this solution is poured into a magnetic agitating stabilizer containing aqueous solution (Shariare *et al*., 2018). The NPs are rapidly formed, and the solvent is separated from the mixture with reduced pressure by the action of rapid solvent diffusion. The approach is used for drugs which are poorly water soluble. The scale, release, and yield of Nano spheres have been shown to be affected by changing the preparation parameters. To formulate smaller Nano spheres, the modification of the polymer concentration in organic solution is found to be useful with a restricted range of polymer to drug ratios (Taarji *et al*., 2022).

D. Polymerization Method. In this method, monomers are polymerized in an aqueous solution as Nanoparticles After polymerization. The drug is either absorbed into the NPs or incorporated, dissolved, into the polymerization media. The Nanoparticles suspension is then refined to remove different stabilizer's and surfactants used to ultracentrifuge and re-suspend particles for polymerization (Rabinow, 2004).

E. Ionic Gelation Method. The process involves precipitation of polymer with an organic phase and the organic layer is then diffused into the aqueous phase with or without surface-active compounds. Biodegradable and hydrophilic polymers, such as gelatin, sodium alginate, and chitosan, are created utilizing a coacervation process for the preparation of NPs. The first hydrophilic chitosan NPs were prepared by Calvo and Janes using two aqueous phases and the ionic gelation technique (Singh and Lillard 2009). The first phase consists of chitosan polymers and diblock co-polymer such ethylene or propylene oxide, and chitosan dissolved in analytical acetic acid with or without a stabilizer. Polyanioncontaining sodium tripolyphosphate is present in the second phase. After mixing the two phases, an interaction between an electrically negative loaded tripolyphosphate and an electropositive loaded amino group of chitosan results in at the nanometer level coacervates (Anandhakumar *et al*., 2017). The ratio of chitosan and stabilizer effects surface charge of particles.

F. Salting Out Method. Based on the extraction of the water-mixable solvent from the aqueous phase by the salting-out effect, salting out is a very closely related procedure for solvent diffusion. This procedure doesn't include any toxic solvents. Acetone is commonly used Because it is entirely miscible and simple to extract from water. Salt produced by aqueous phase saturation using colloidal stabilizers, emulsion stabilizers, and viscosity increasing agents such as polyvinylpyrrolidone or hydroxyethyl cellulose, PVA, polyethylene (ethylene), and polypropylene (Zielinska *et al.*, 2020). Polymers and drugs have been dissolved in a solvent that has emulsified into an aqueous solution containing salt-induced precipitants (e.g., electrolytes and trimethylene carbonate). Oil in water emulsion (o/w) was prepared, and then it was diluted with enough water to permit complete diffusion of acetone penetration into the water phase, inducing the production of nanospheres. This method not require need for higher temperatures and stirring energy required for lower particle sizes (Mohanraj and Chen 2007).

G. Dialysis. Dialysis is an effective technique for NP preparation. In this approach, the drug and polymer are dissolved in organic solvent, like Poly (benzyl-l-glutamate)-b-Poly (ethylene oxide) or Poly(lactide)-b-Poly (ethylene oxide). This organic mixture was introduced to a dialysis tube, and the dialysis was performed using the former mixable as a buffer against a non-solvent. This organic mixture was introduced to a dialysis tube, and the dialysis was performed using the former mixable as a buffer against a non-solvent (Alavi and Nokhodchi 2020). This method involves the displacement of the solvent system within the dialysis membrane, which is followed by a gradual

accumulation of polymer, which reduces its solubility and causes the creation of NPs in a homogenous suspension form (Pal *et al*., 2011).

Characterization of NPs

1. Percentage Yield of NPs. Nanoparticles were collected and weighed accurately. The percentage (%) yield was then calculated using formula given below

$$\%\text{Yield} = \frac{\text{Mass of nanoparticles obtained}}{\text{Total weight of drug and polymer}} \times 100$$

2. Entrapment Efficiency of NPs. This evaluation parameter gives idea about the percentage drug that is successfully adsorbed or entrapped into NPs. The weighed amount of NPs is dissolved in an appropriate solvent, then centrifuged for analysis. Following centrifugation, then the UV spectrophotometer is used to measure the amount of API in the supernatant (w), and a standard calibration curve is then constructed (Muruganantham *et al*., 2021). The amount of APIs in the liquid supernatant is then deducted from the total amount of APIs used to make the NPs. Then quantity of drug is entrapped in prepared Nanoparticle's are determined. Percentage (%) API entrapment calculated by

$$\%\text{ Entrapment Efficiency} = \frac{\text{Total amount of drug added} - \text{Nonbound drug}}{\text{Total amount of drug}} \times 100$$

1. Size and Size Distribution of Particles. The solubility, reaction, and dissolution rates, as well as the physical stability and biological activity of the NPs, are all impacted by the size distribution of the particles. Dynamic light scattering (DLS), photon correlation spectroscopy (PCS), laser diffraction spectroscopy (LDS), and a Coulter counter multi-sizer can all be used to assess it (CCM) (Lohat *et al*., 2020).

2. Zeta Potential Analysis. NP formulation particle charge is determined using a zeta analyzer device. In order to comprehend the condition and long-term stability of the surface charge characteristics of NPs, this study provides some data. Because of stronger electrostatic attraction between the particles, particles with larger zeta-potentials exhibit improved stability (Crucho and Barros 2017). For dd (electrostatic repulsion) stabilized NPs, a zeta potential of at least 30 mV is expected, but a zeta potential of 25 mV would be sufficient in the case of integrated electrostatic and steric stabilizer.

Releasing Mechanism of Active Agent from OFDFs: The oral mucosa is highly vascularized and thin therefore it is very permeable to absorbed drugs in the systemic circulation an effective approach. As a result, using a penetration enhancer may not be necessary. Oral films are simply films applied to the tongue or buccal cavity of a patient. due to the presence of a water-soluble polymeric ingredient and other excipients in the film, instantly becomes hydrated by saliva it contains 99% water. After passing through the oral mucosa and being absorbed into the reticulated and jugular veins(Xiao *et al*., 2013), the hydrated film quickly breaks to release the active ingredient, which causes the medicine to be emptied into the systemic circulation.

Composition of oral film:

1. Active Pharmaceutical ingredients
2. Film-forming polymer
3. Plasticizer
4. Saliva stimulating agent
5. Sweetening agent
6. Surfactant
7. Flavors
8. Coloring agent

Table 1: Composition of oral film.

Ingredients	Amount
Active Pharmaceutical ingredients	5 - 30 %
Film-forming polymer	45 %
Plasticizer	1 -20 %
Saliva stimulating agent	2 - 6 %
Sweetening agent	3 - 6 %
Surfactant	q.s
Flavors, coloring agent	q.s

A. Active Pharmaceutical ingredients. There are selections of API on the basis of its potency, dose and therapeutic efficacy. Mostly favorable APIs for oral film include antianginal, antiepileptic, antitussive, hypnotic, sedative antihistaminic, expectorant, analgesic, anti-allergic. etc.(Borges *et al*., 2015).

B. Film-forming polymer. The polymer used as film former are should provide rapid disintegration and good mechanical strength to films. The texture of film depends on type of polymer and concentration in the formulation. Water soluble polymer containing oral film adheres to buccal mucosa and rapidly delivers drug into systematic circulation which causes rapid onset of action (Kulkarni *et al*., 2021). The wide variety of polymer used for the preparation of oral film which HPMC K4M, HPMC K15, gelatin, pullulan, modified starch, hydroxyl ethyl cellulose, guar gum, xanthum gum, in Table 2 etc. the total weight of dry film contains at least 45%w/w of polymer.

Table 2: Classification of film forming polymer.

Sr. No.	Class	Polymers
1.	Carbohydrate	Sodium alginate, metodextrine, pullulan (Pacheco *et al*., 2021)
2.	Protein	Gelatin
3.	Cellulose derivatives	Hydroxy propyl methyl cellulose (E3, E5, E15, K3, K15, K50), Microcrystalline cellulose, Caroscarmellose Sodium
4.	Acrylpolymer	Eudragit (RD-9, 10, 11, 12, 100 and RL-100)
5.	Vinyl polymer	Poly vinyl pyrrolidone (K90, K30), Poly vinyl alcohol, poly ethylene oxide.

C. Plasticizers. It is vital ingredient in an oral film which is considered flexibility of film by reducing its brittleness and improving mechanical properties such as tensile strength, folding endurance and elongation of film. The selection of plasticizer based upon its compatibility with polymer and solvent used for film formulation. concentrations of plasticizers affect physical properties and absorption rate also of film therefore typically 1-20% concertation of dry plasticizers used in film. Inappropriate use of plasticizers in a film may causes cracking, blooming, pilling and uneven splitting of film. Examples, Low molecular weight polyethylene, glycols ,Glycerol, Propylene glycol, Citrate derivatives like acetyl citrate, Phthalate derivatives liked butyl derivatives dimethyl, diethyl, diethyl, Castor oil etc.(Bhattarai and Gupta 2015).

D. Saliva stimulating agent. The main purpose of saliva stimulating agent is to enhance the production of saliva that would help in the rapid dissolution of oral film. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric are the few examples of salivary stimulant which used to stimulate salivary secretion in oral cavity (Sultana *et al.*, 2013). Saliva stimulating agent used alone as well as combination between 2 to 6% w/w of the weight of dry film.

E. Sweetening agent. Sweetener are essential ingredients in pharmaceutical dosage forms used to dissolved in oral cavity (Karki *et al.*, 2016). sweet dosage form is important in pediatric population. Natural and Artificial sweeteners are intended to improved palatability of oral dissolving formulation. Commonly used alone or combination between the concentration of 3 to 6%w/w. below some are example of sweeteners:

a) Water soluble artificial sweeteners: sodium or calcium saccharin salts, cyclamate salts, acesulfame-k etc.

b) Water soluble natural sweetener (Tiwari *et al.*, 2018): xylose, ribose, glucose, sucrose, maltose, sativoside etc.

c) Dipeptide based sweetener: aspartame

E. Flavoring Agent. USFDA approved flavors will be used to masking the bitter taste of oral formulation. The quantity of flavor to be added to mask the taste mainly relate to the flavor strength and its type. The formulation contains a flavoring compound at a concentration of 10% w/w. US-FDA approved flavor can be added to the formulation according the preferences of people in various age groups. The flavors changes with the age (Sevinç Özakar and Özakar 2021). geriatric population like mint or orange flavors, while younger generations prefer strawberry, fruit, and raspberry flavors. Flavoring agent must be compatible with the drug as well as other ingredients. Flavoring agent can be extracted from different part of the plant including fruit, leaves, flowers, fruit, seeds, and bark, can be used as sources of flavoring agents.

G. Coloring Agent. FD & C approved coloring agent is incorporated in oral film at concentration of level of not more than 1%w/w coloring agent used are EU colors ,natural colors ,and custom Pantone –matched colors for example, titaniumoxide, siliconoxide, zinc dioxide (Rajni Bala *et al*., 2013).

H. Surfactant. Surfactants are employed as wetting, dispersing, and solubilizing agents to so the film gets dissolved within seconds and release active agent rapidly. Surfactants are improve the solubility of poorly soluble drugs in oral films(Arya *et al.*, n.d.). These are some examples likepolaxamer 407, sodium lauryl sulfate, benzalkonium chloride, benzthonium chloride, tweens and spans etc.

Methods used for manufacturing oral film: Following are methods used for manufacturing oral film.

(i) Solvent casting method
(ii) Semisolid casting method
(iii) Hot melt extrusion
(iv) Solid dispersion extrusion
(v) Rolling method

1. Solvent Casting Technique (Choudhary *et al.*, 2012). Fast-dissolving films are typically created using the solvent casting method, in which the water-soluble ingredients are combined to create a clear, viscous solution, the drug and other excipients are dissolved in an appropriate solvent like ethanol. After mixing the two solutions, the Petri plate is cast, dried, and then cut into the desired-sized pieces. The characteristics of the API are quite important when choosing a good solvent. Typically, bases for film casting are made of glass, plastic, or Teflon plates. Cutting, stripping, and packaging are done once the films have dried. It is possible to cut films into the required sizes and shapes. 3×2 cm^2 and 2×2 cm^2 are the most popular film sizes.

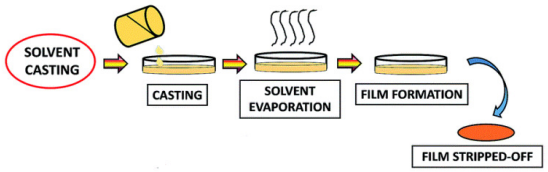

Fig. 1. Solvent Casting technique.

2. Semisolid casting (**Thakur *et al.*, 2012).** A water-soluble film-forming polymer solution is initially formulated in the semisolid casting process. The result and a fix are merged. Drying the film is the last process, which helps to generate the final product by getting rid of the solvent. Film casting frequently starts on plates made of glass, plastic, or Teflon After that, the proper quantity of plasticizer is added to prepare a gel mass. Finally, using heat-controlled drums, the gel mass is cast into the films or ribbons cutting, stripping, and packaging are completed after the films have dried.

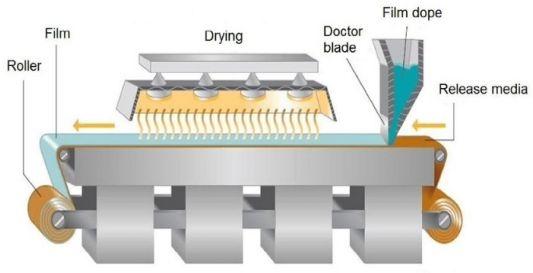

Fig. 2. Semisolid casting.

It is possible to cut films into the required sizes and shapes. The film is between 0.015 and 0.05 inches thick. The ratio of film-forming polymer to acid-insoluble polymer should be 1:4.

3. Hot melt extrusion (Pimparade *et al.*, 2017). Granules, sustained-release pills, and transdermal and trans mucosal drug delivery systems are frequently formulated via hot melt extrusion. In the hot melt extrusion procedure, the drug and carriers are first combined in solid form. The mixture is then melted by a heater-equipped extruder. Finally, the dies form the melt into films. Typically, low molecular weight or viscosity polymers, such pullulan PI.20 or HPMC E5, are preferred in oral film. To obtain desired physical qualities, several grades of polymers may also be combined. A film with superior mechanical strength and high drug solubility in the film is produced by combining polymers with high and low viscosities.

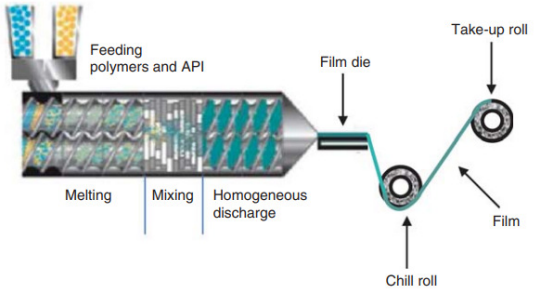

Fig. 3. Hot melt extrusion.

4. Rolling method (Panda *et al.*, 2012). The film is prepared by pre-mixing an active ingredient, and then forming the film. Prepare the pre-mix with the exception of a drug, polar solvent, film-forming polymer, and other additions. Fill the master batch feed tank with premix. A first metering pump and control valve fed it to either the first mixer or both the first and second mixers. Then, add the necessary amount of drug to the chosen mixer. To prepared a consistent matrix, combine the drug with the master batch's pre-mix. Following a certain amount of uniform being measured out using a second meter, pumps are used to feed the matrix into the pan. Finally, the film is prepared on the substrate and removed by the support roller. After that, bottom drying will be used to dry the wet film. By weighing each of the 10 randomly chosen oral films individually and figuring out their average weight, weight variation is analyzed.

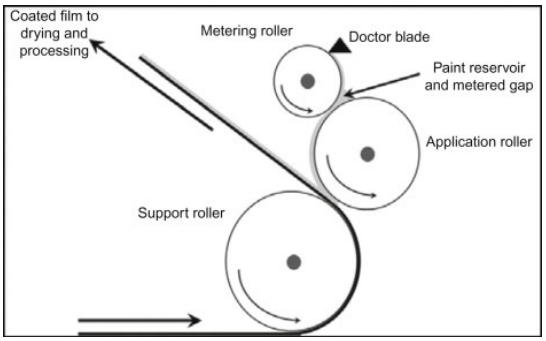

Fig. 4. Rolling method.

EVALUATION OF NANOPARTICLE LOADED ORAL DISSOLVING FILMS

(a) Weight variation. By weighing each of the 10 randomly chosen oral films individually studied out their average weight and weight variation is analyzed (Patil *et al.,* 2014).

(b) Thickness. The film thickness is directly relates to Uniformity of drug content, so it is important to Check for uniformity in the film's thickness(Aditya and Nagarsenker 2008). At different sites, it could be measured using a Micro screw gauge or digital Vernier calipers.

(c) Tensile strength. When a strip is put to a film break of specimens, the maximum pressure is exerted at that point. It is computed by dividing the load acting on the rupture by the area of the strip's cross section (Phalguna *et al.*, 2019; Miles *et al.,* 2016).

(d) Percent elongation. A sample of the film stretches when stress is applied, and this is known as strain. In essence, strain is film deformation divided by the initial dimension of the sample. Film elongation increases as plasticizer content does (Latif and Ashfaq 2019).

$$\% \text{ Elongation} = \frac{\text{Increase in length}}{\text{Original length}} \times 100$$

(e) Folding endurance. Repeated film folding at the same point until the filling breaks is used to measure folding endurance. The number of times the film will be folded without breaking is measured, and the folding endurance % is then determined (Upreti *et al*., 2014).

(f) Content uniformity (Londhe and Shirsat 2018). Any standard method of assay specified in any of the standard pharmacopoeia for a specific API has established this. Estimating the Individual film API content yields information about the regularity of the content. The acceptable range for content uniformity is 85% to 115% in oral film.

(g) Disintegration time (Rathore *et al.*, 2019). Fast-dissolving oral films must be disintegrated using a US disintegration apparatus. Oral film should not disintegrate for more than 30 seconds at a time. Fast dissolving oral films can use the oral disintegrating tablet outlined in Centre for Drug Evaluation and Research (CDER) guidance. Depending on the formulation, disintegration times can vary, although they commonly in between 5 and 30 seconds.

(h) Dissolution test (Hiwse *et al.*, 2022). Dissolution testing is carried out using a USP Π standard paddle or basket apparatus at 37±0.5°C and 50 rpm speed prescribed in pharmacopoeia. The high dose of the API and sink conditions will be taken into phosphate buffer (pH 6.8) dissolution medium. The tendency of the film to float when the paddle device is used onto the dissolving media makes the dissolution test difficult so often.

(i) Swelling property. Using a simulated saliva solution, studies on film swelling are carried out. Each test film is weighed and placed into a pre-weighed stainless steel mesh wire, which is then dipped in a 15 ml medium in a plastic container. At each pre-set time interval like 60, 120, 180 sec and weight of the film increased until a steady weight was noticed (Salama *et*

al., 2021). When determining the degree of swelling index, parameters are used.

Swelling index = $(W_t - W_0)/W_0$

Where,

Wt = weight of film at time t, Wo =weight of film at time zero.

CONCLUSIONS

The benefits of including NPs loaded oral film have been examined in this paper. This data demonstrates that it is feasible to make films containing NPs with suitable physical-mechanical properties in a single formulation process. Encapsulating active components in Nano materials has been used to increase the stability and permeability of bio macromolecules and reduce their toxicity. NPs can thus be easily converted to oral films and are amenable to being prepared to alter the pharmacokinetic profile of active pharmaceutical ingredients.

In order to transform unstable physiologically active molecules into promising deliverable pharmaceuticals, difficulties associated with poorly soluble or insoluble lipophilic drug in both organic and aqueous phases must be properly addressed. Additionally, advancements are required to turn the Nano-oral film technology hypothesis into a workable, real-world strategy as the next generation of drug delivery systems. The suggested method may improve patient compliance by increasing solubility and permeability in oral mucosa. This analysis leads us to the conclusion that Nano particle loaded oral film is promising drug delivery system for poorly water soluble and low permeability drug by solving problems associated with it by increasing bioavailability.

FUTURE SCOPE

The nanotechnology to oral solid films can increase the bioavailability of medications while providing effective therapeutic results. Additionally, because oral films are simple to use, fabricate, appealing, and simplify the dose routine, medication adherence is improved. Pharmaceutical companies are now utilizing oral film advantages and growing acceptance by formulating various active pharmaceutical ingredients (APIs) as films to enhance patient outcomes. Considering the future, more drug being loaded Nano particle incorporated in oral films.

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Conflict of Interest. None.

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