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Oral Fast Dissolving Films of Promethazine Hydrochloride Employing Natural Surfactants: A Comprehensive Review of Formulation Science, Pharmacology and Evaluation Strategies

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Abstract- ***Oral fast dissolving films (OFDFs) have emerged as one of the most patient-centric advances in solid-dosage drug delivery, dissolving within seconds on the tongue without the need for water and thereby resolving the swallowing difficulties that beset paediatric, geriatric, bedridden and non-cooperative populations. Promethazine hydrochloride, a first-generation phenothiazine antihistamine with potent antiemetic and sedative activity, is an attractive candidate for film-based delivery because its conventional oral formulations suffer from extensive hepatic first-pass metabolism (absolute bioavailability ≈ 25%), delayed onset of action and an intensely bitter taste that compromises compliance. This review consolidates current knowledge on the design of promethazine OFDFs, with particular emphasis on the substitution of synthetic surfactants by biocompatible natural surfactants such as lecithin and triterpenoid saponins. The physiology of oral mucosal absorption and of the emetic reflex is examined to justify the rapid-onset rationale, followed by a detailed drug profile, a survey of film-forming polymers and functional excipients, the mechanistic basis of surfactant-mediated solubility enhancement, the principal manufacturing techniques, and the complete battery of physicochemical, mechanical and biopharmaceutical evaluation parameters. Illustrative analytical data, recent literature and global market trends are presented graphically. Natural-surfactant OFDFs of promethazine represent a green, biocompatible and commercially relevant strategy for achieving rapid antiemetic relief, although challenges in drug loading, taste masking and large-scale reproducibility remain to be fully addressed.***

Keywords: Oral Fast Dissolving Film, Promethazine Hydrochloride, Natural Surfactant, Lecithin, Saponin, Solvent Casting, Antiemetic, Bioavailability, Taste Masking.

I. INTRODUCTION

The oral route remains the most widely accepted pathway for drug administration owing to its convenience, non-invasiveness, dosing flexibility and high patient acceptance. Conventional solid oral dosage forms—tablets and capsules—nevertheless present a recurring clinical limitation: a substantial proportion of patients experience dysphagia, the difficulty or inability to swallow. This problem is most pronounced in children, the elderly, bedridden individuals, psychiatric patients and travellers who lack ready access to water, and it directly translates into reduced adherence and therapeutic failure. The pharmaceutical response to this unmet need has been the development of orally disintegrating dosage forms, of which the oral fast dissolving film (OFDF) is the most recent and arguably the most elegant expression [1, 4].

An OFDF is a thin, postage-stamp-sized strip composed predominantly of hydrophilic, film-forming polymers that hydrates instantaneously upon contact with saliva and disintegrates, releasing its drug load within seconds. Because no water is required and because the film adheres briefly to the moist mucosa, the dosage form combines the dosing accuracy of a tablet with the ease of administration of a liquid [7,

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35]. Drugs delivered through the buccal or sublingual mucosa may also partly escape hepatic first-pass metabolism, entering the systemic circulation directly through the highly vascularised oral epithelium and so achieving a faster onset of action and potentially improved bioavailability [3].

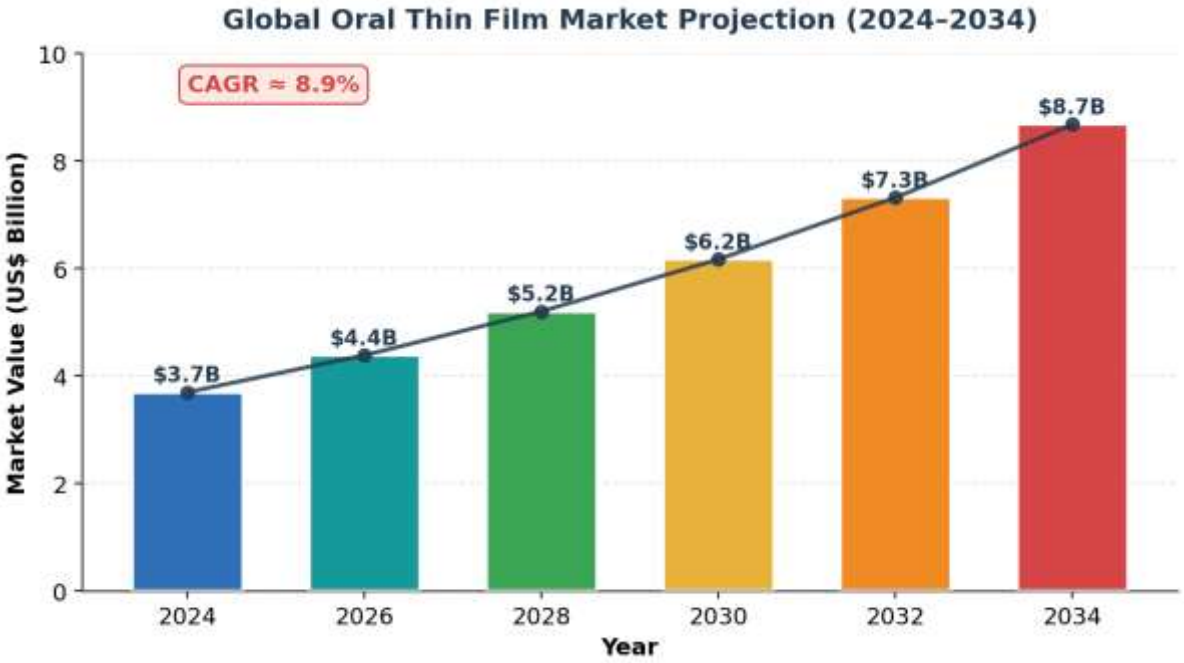

Figure 1. Projected growth of the global oral thin film market, 2024–2034, reflecting strong and sustained commercial demand for film-based dosage forms.

The commercial trajectory of these systems underscores their clinical relevance. The global oral thin film market was valued at approximately US$3.7 billion in 2024 and is forecast to expand at a compound annual growth rate of close to 8.9%, reaching an estimated US$8.7 billion by 2034 (Figure 1) [18]. Growth is being driven by an ageing global population, rising paediatric demand, advances in polymer science and a broader industry shift toward patient-centric care. The Asia-Pacific region—led by manufacturing expansion in India and China—is projected to be the fastest-growing segment, expanding at over 10% annually [18].

Promethazine hydrochloride is a logical candidate for this delivery platform. As a first-generation phenothiazine antihistamine, it is widely prescribed for the prophylaxis and treatment of nausea and vomiting associated with motion sickness, post-operative recovery and chemotherapy, as well as for allergic conditions and as a sedative [8, 9]. Yet its conventional tablet and syrup formulations are constrained by an absolute oral bioavailability of only around 25% due to extensive first-pass hepatic metabolism, by a comparatively slow onset, and by an intensely bitter taste that markedly reduces compliance, particularly among the very paediatric and geriatric groups for whom rapid antiemetic relief is most often required [10, 25]. A fast-dissolving film that delivers promethazine rapidly across the oral mucosa therefore addresses several of the drug's principal pharmaceutical shortcomings simultaneously.

A further dimension explored in contemporary formulation research is the replacement of conventional synthetic surfactants with natural surfactants. Surfactants are incorporated into OFDFs to improve the wetting, solubilisation and dissolution of poorly soluble actives. Natural surfactants such as soy lecithin and plant-derived triterpenoid saponins offer biocompatibility, biodegradability and low toxicity relative to many synthetic alternatives, aligning film development with the wider movement

toward green, renewable pharmaceutical excipients [15, 16]. This review brings together the pharmacological, physicochemical and technological knowledge underpinning the rational design of natural-surfactant OFDFs of promethazine hydrochloride, and presents illustrative analytical data to frame the discussion.

A. Advantages and Limitations of Oral Fast Dissolving Films

The clinical and commercial momentum behind OFDFs derives from a distinctive cluster of advantages. They are administered without water, an attribute of obvious value to travellers, bedridden patients and those with restricted fluid intake. They disintegrate within seconds, giving a faster onset of action than conventional tablets that must first disintegrate and dissolve in the gastrointestinal tract. They improve compliance in paediatric and geriatric populations who struggle to swallow solid dosage forms or who fear choking. Because a portion of the dose is absorbed across the buccal and sublingual mucosa, the dosage form can partly bypass hepatic first-pass metabolism, improving bioavailability for drugs that are otherwise extensively metabolised. Their large surface-to-volume ratio favours rapid hydration and dissolution, and their flexible, flat geometry confers good portability, accurate unit dosing and ease of handling relative to fragile orally disintegrating tablets [7, 33, 34].

These benefits are balanced by genuine limitations that shape formulation strategy. The thin geometry and the small volume of saliva available restrict the drug load that can be incorporated and dissolved rapidly, making high-dose drugs difficult to deliver as a single film. Drugs with an unpleasant or bitter taste, of which promethazine is a prominent example, require effective taste masking that must not compromise disintegration or release. The high surface area that aids dissolution also renders films sensitive to atmospheric moisture, demanding protective, moisture-resistant packaging and careful stability management. Dose uniformity can be challenging to maintain during high-throughput casting and cutting, and the cost of specialised manufacturing and packaging equipment can be significant. A clear appreciation of this advantage–limitation balance is essential to the rational design of a successful promethazine film [30, 34].

II. ANATOMY AND PHYSIOLOGY OF ORAL MUCOSAL DRUG ABSORPTION

A rational understanding of OFDF performance begins with the oral cavity as an absorptive surface. The oral mucosa is lined by stratified squamous epithelium that varies regionally in keratinisation and permeability. The sublingual region (the floor of the mouth) and the buccal region (the inner cheek) are non-keratinised, relatively thin and richly vascularised, making them favourable sites for drug permeation. Blood draining from these tissues enters the systemic circulation via the lingual, facial and retromandibular veins, ultimately reaching the internal jugular vein—crucially, bypassing the hepatic portal system and therefore avoiding the hepatic first-pass metabolism that degrades so much of an orally swallowed dose [3, 35].

The sublingual mucosa is the most permeable oral site and supports rapid onset, making it ideal for drugs requiring immediate action. The buccal mucosa, while somewhat less permeable, offers a larger and more stable surface that is better suited to longer residence times. Transport across these membranes occurs predominantly by passive diffusion, the rate of which is governed by the drug's lipophilicity, degree of ionisation at salivary pH (approximately 6.8), molecular size and the local concentration gradient. Promethazine, with a log P of about 3.7 and favourable membrane penetration, is well suited to passive paracellular and transcellular transport across the oral epithelium [10].

Saliva itself is integral to film performance. A healthy adult secretes roughly 0.5 to 1.5 litres of saliva daily; this fluid hydrates the hydrophilic polymer matrix, triggers disintegration and provides the aqueous medium in which the drug dissolves before absorption. The limited volume of saliva available at any instant, however, imposes a practical ceiling on the drug load that a single film can carry while still dissolving rapidly and completely—an important constraint in formulation design that is revisited later in this review.

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III. EMESIS: PATHOPHYSIOLOGY AND THE RATIONALE FOR RAPID ANTIEMETIC DELIVERY

Emesis, or vomiting, is the forceful retrograde expulsion of gastric contents through the mouth. It is a protective reflex that rids the body of ingested toxins, but when triggered inappropriately—by motion, drugs, surgery or chemotherapy—it becomes a distressing and clinically significant symptom. The reflex is coordinated by the vomiting centre, a diffuse network of neurons in the lateral reticular formation of the medulla oblongata, which integrates afferent signals from several distinct sources (Figure 2) [9].

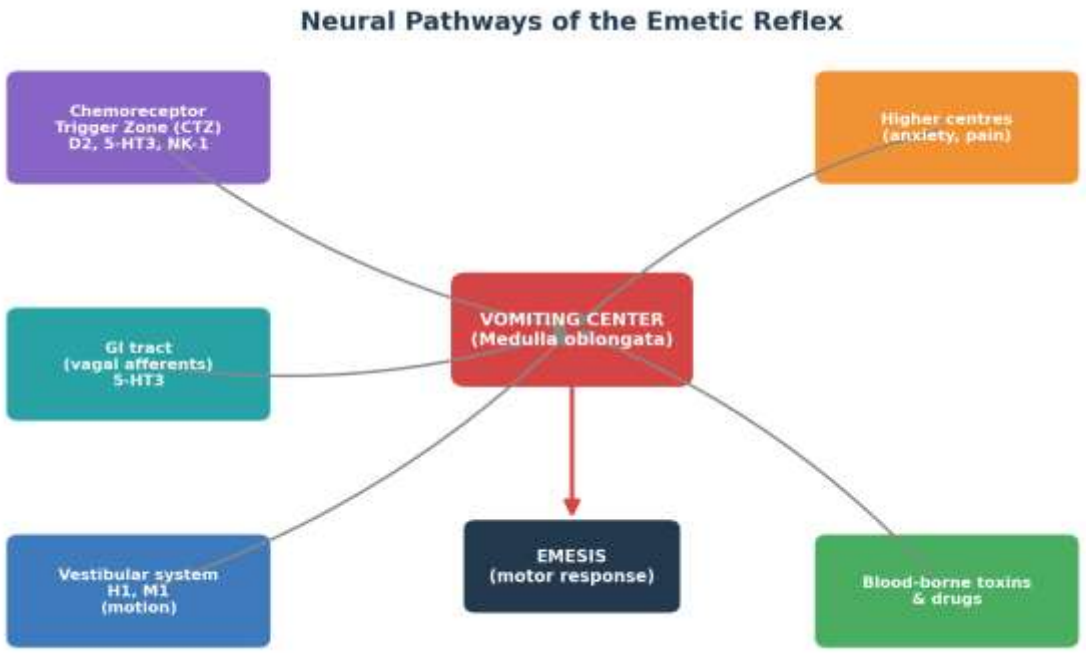

Figure 2. Convergent neural pathways of the emetic reflex. The medullary vomiting centre integrates inputs from the chemoreceptor trigger zone, gastrointestinal tract, vestibular system and higher cortical centres, each mediated by characteristic neurotransmitter systems that constitute antiemetic drug targets.

The chemoreceptor trigger zone (CTZ), located in the area postrema at the floor of the fourth ventricle, lies functionally outside the blood–brain barrier and is therefore exposed to emetogenic substances circulating in the blood and cerebrospinal fluid. It is densely populated with dopamine (D2), serotonin (5-HT3) and neurokinin-1 (NK-1) receptors. The gastrointestinal tract contributes through vagal and splanchnic afferents that respond to mucosal irritation, distension and the release of serotonin from enterochromaffin cells. The vestibular apparatus of the inner ear signals through histaminergic (H1) and muscarinic (M1) pathways and is the principal driver of motion sickness. Higher cortical and limbic centres relay anticipatory nausea, anxiety and pain [9, 13].

The neurotransmitters mediating these pathways define the pharmacological targets of antiemetic therapy. Serotonin acting on 5-HT3 receptors, dopamine on D2 receptors, substance P on NK-1 receptors, and histamine and acetylcholine within the vestibular pathway each provide a point of therapeutic intervention. Promethazine exerts its antiemetic action principally through central H1-receptor antagonism, with contributions from muscarinic blockade and weak dopaminergic antagonism, making it especially effective against vestibular and motion-related nausea [9, 14].

Because nausea and vomiting frequently demand immediate relief—a traveller experiencing acute motion sickness, a post-operative patient, or a child

unable to retain an oral tablet—a dosage form that delivers the antiemetic rapidly and without the need to swallow water offers a distinct clinical advantage. The OFDF, dissolving in seconds and releasing drug for pre-gastric absorption, is therefore particularly well matched to the therapeutic requirements of antiemetic pharmacotherapy.

IV. PROMETHAZINE HYDROCHLORIDE: DRUG PROFILE

A. Physicochemical Characteristics

Promethazine was first synthesised in 1947 and entered clinical use in the early 1950s, and it has remained in continuous, widespread use ever since; in the United States alone more than 2.5 million prescriptions were written in a single recent year, underlining its enduring therapeutic relevance [10]. Promethazine hydrochloride is the hydrochloride salt of promethazine, a phenothiazine derivative with the molecular formula $C_{17}H_{20}N_2S \cdot HCl$ and a molecular weight of approximately 320.9 g/mol. It is a white to faintly yellow, odourless crystalline powder that is freely soluble in water and in ethanol, a property that simplifies its incorporation into the aqueous or hydroalcoholic casting solutions used for film manufacture. The drug oxidises slowly on prolonged exposure to air, acquiring a blue tint, and is therefore protected from light during processing and storage [8]. It is markedly lipophilic (log P ≈ 3.7), which favours penetration of biological membranes including the oral mucosa and the central nervous system [10].

B. Pharmacodynamics

Promethazine is a competitive antagonist at peripheral and central histamine H1 receptors, an action that underlies its antiallergic and sedative effects. Centrally, blockade of H1 receptors within the vomiting centre and vestibular pathways produces its antiemetic and anti-motion-sickness activity. The molecule additionally exhibits anticholinergic (antimuscarinic) activity, a strong alpha-adrenergic blocking effect and a comparatively weak antidopaminergic action; unlike chlorpromazine and related phenothiazines, it has limited D2 activity and is not used as an antipsychotic [9, 11]. The combined H1 and muscarinic blockade is largely responsible for the drug's effectiveness against the vestibular component of nausea.

C. Pharmacokinetics

Following oral administration, roughly 80 to 90% of a promethazine dose is absorbed from the gastrointestinal tract; however, the drug undergoes extensive hepatic first-pass metabolism—principally hydroxylation via CYP2D6 and N-demethylation via CYP2B6, with sulfoxidation and glucuronidation—so that its absolute oral bioavailability is reduced to only about 25% [11, 12, 14]. Peak plasma concentrations after oral dosing occur at approximately 1.5 to 3 hours. The drug is highly bound to plasma proteins (around 90 to 95%), has a large volume of distribution (4 to 8 L/kg) and a terminal elimination half-life of roughly 10 to 19 hours. Its major metabolites, promethazine sulfoxide and N-demethylpromethazine, are largely inactive and are eliminated in the urine [10, 13]. The variability and inefficiency of oral absorption, set against the comparatively higher bioavailability achievable by parenteral and pre-gastric routes, provide the central pharmacokinetic rationale for film-based delivery (Figure 3).

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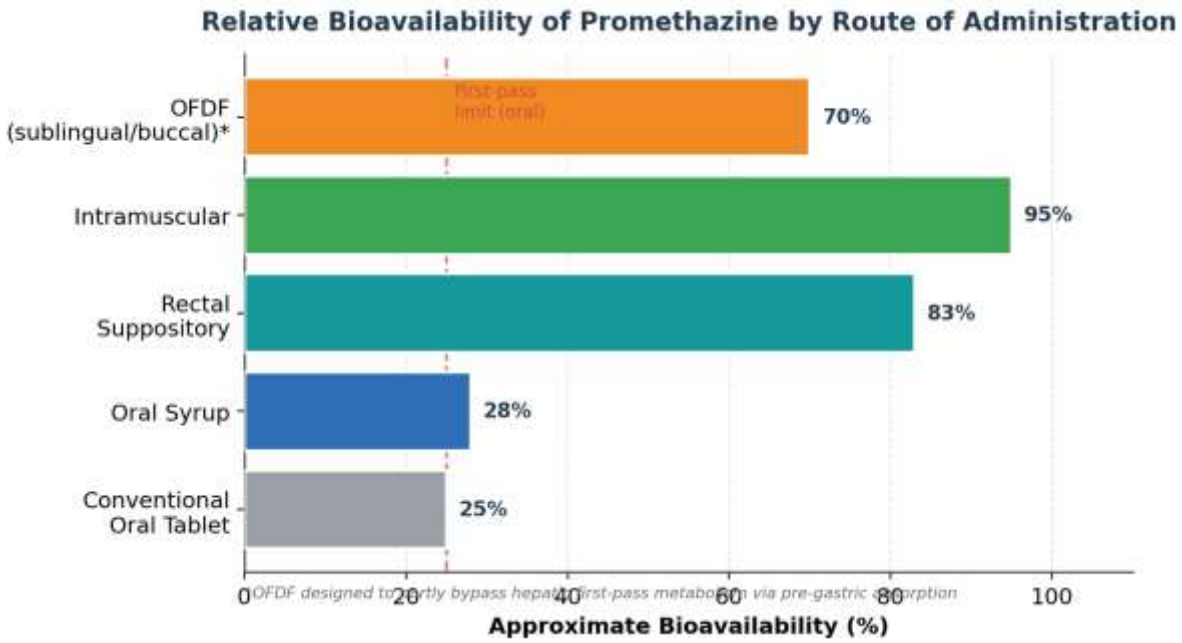

Figure 3. Approximate relative bioavailability of promethazine by route of administration. Conventional oral dosing is severely limited by first-pass metabolism (≈25%); film-based pre-gastric delivery is designed to partly circumvent this barrier.

D. Therapeutic Uses and Limitations

Clinically, promethazine is employed for the prevention and treatment of nausea and vomiting of diverse aetiologies—motion sickness, post-operative emesis and chemotherapy-induced nausea—and as an antihistamine in the management of allergic conditions, as well as for sedation and as an adjunct in pain management [9]. Despite this versatility, the conventional formulations have well-documented limitations. The intensely bitter taste of the drug, with a reported bitterness recognition threshold of approximately 10 micrograms per millilitre detectable within thirty seconds, substantially reduces palatability and adherence, especially in children [25]. The slow and variable onset of conventional oral dosing is a further drawback when rapid relief is needed. These constraints make promethazine an instructive model drug for the development of taste-masked, rapidly disintegrating film formulations, and they explain the considerable research attention the drug–delivery combination has attracted.

V. ORAL FAST DISSOLVING FILMS: CONCEPT AND COMPOSITION

An ideal OFDF should possess a pleasant taste, adequate mechanical strength for handling and packaging, rapid and complete disintegration in the oral cavity, good content uniformity and acceptable stability. Achieving these often competing attributes depends on the careful selection and balancing of several classes of excipient, each contributing a defined function to the final film (Figure 4) [7, 34].

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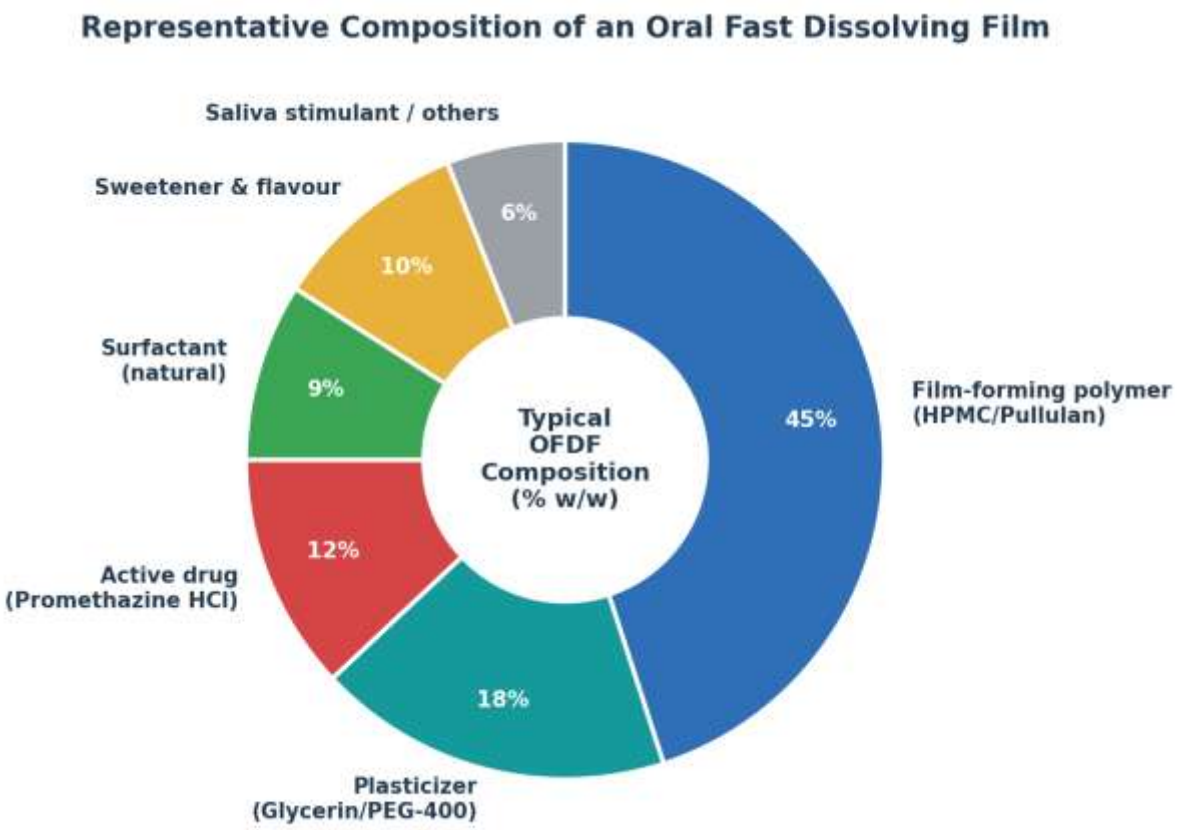

Figure 4. Representative quantitative composition of a typical oral fast dissolving film, dominated by the film-forming polymer with supporting plasticiser, surfactant, drug and palatability excipients.

A. Film-Forming Polymers

The film former constitutes the structural backbone of the dosage form, typically accounting for 40 to 50% of the dry film mass, and its choice governs film integrity, flexibility, dissolution rate and mouthfeel. Hydroxypropyl methylcellulose (HPMC) is the most widely used polymer, valued for its excellent film-forming ability, water solubility, transparency and capacity to produce flexible films; lower-viscosity grades such as HPMC E5 and E15 are favoured for fast-dissolving applications [21, 22]. Pullulan, a naturally occurring linear polysaccharide produced by the fungus Aureobasidium pullulans, is increasingly preferred because of its rapid hydration, neutral taste, excellent oxygen barrier, mechanical strength at thin gauges and its plant-derived, vegan-compatible credentials; it is recognised in the USP, EP and JP pharmacopoeias and forms a key part of the rapidly expanding film-polymer market [25, 28]. Polyvinyl alcohol (PVA) imparts flexibility and accelerates dissolution, while gellan gum and other natural gums contribute gel-forming and mucoadhesive properties. The judicious blending of natural and synthetic polymers allows formulators to tune disintegration time, tensile strength and folding endurance to target specifications [23, 24].

B. Plasticizers

Plasticizers, generally incorporated at 5 to 20% of the polymer weight, reduce the glass transition temperature of the polymer and confer the flexibility necessary to prevent cracking during manufacture, packaging and handling. Glycerin (glycerol), polyethylene glycol 400 (PEG-400) and propylene glycol are the most commonly employed. The type and concentration of plasticizer exert a pronounced influence on the mechanical profile of the film: increasing plasticizer content typically raises percentage elongation and folding endurance while reducing tensile strength, allowing a deliberate trade-off between pliability and rigidity [21, 35].

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C. Surfactants and Functional Excipients

Surfactants improve the wettability of the film and enhance the solubilisation and dissolution of the active, an effect central to the present review and discussed in detail in Section 6. Beyond surfactants, palatability excipients are indispensable for a dosage form held in the mouth. Sweeteners such as sucralose, aspartame and mannitol, together with flavouring agents (mint, citrus, fruit) and colourants, mask residual bitterness and improve acceptance, particularly for a markedly bitter drug such as promethazine [25, 35]. Saliva-stimulating agents—citric, malic, ascorbic and tartaric acids—accelerate film hydration by promoting salivation, and their incorporation can meaningfully shorten disintegration time. Together these excipients transform an otherwise unpalatable strip into a patient-friendly product.

VI. NATURAL SURFACTANTS IN FILM FORMULATION

Surfactants are amphiphilic molecules possessing both hydrophilic and hydrophobic domains, enabling them to lower surface and interfacial tension, promote wetting and self-assemble into micelles that solubilise poorly water-soluble drugs. In OFDFs they improve the uniform distribution of the active within the polymer matrix and accelerate its release upon contact with saliva. Although synthetic surfactants such as sodium lauryl sulfate (SLS) and the polysorbates are effective and widely used, concerns over their potential for mucosal irritation, limited biocompatibility and environmental persistence have driven interest in natural alternatives [15, 17].

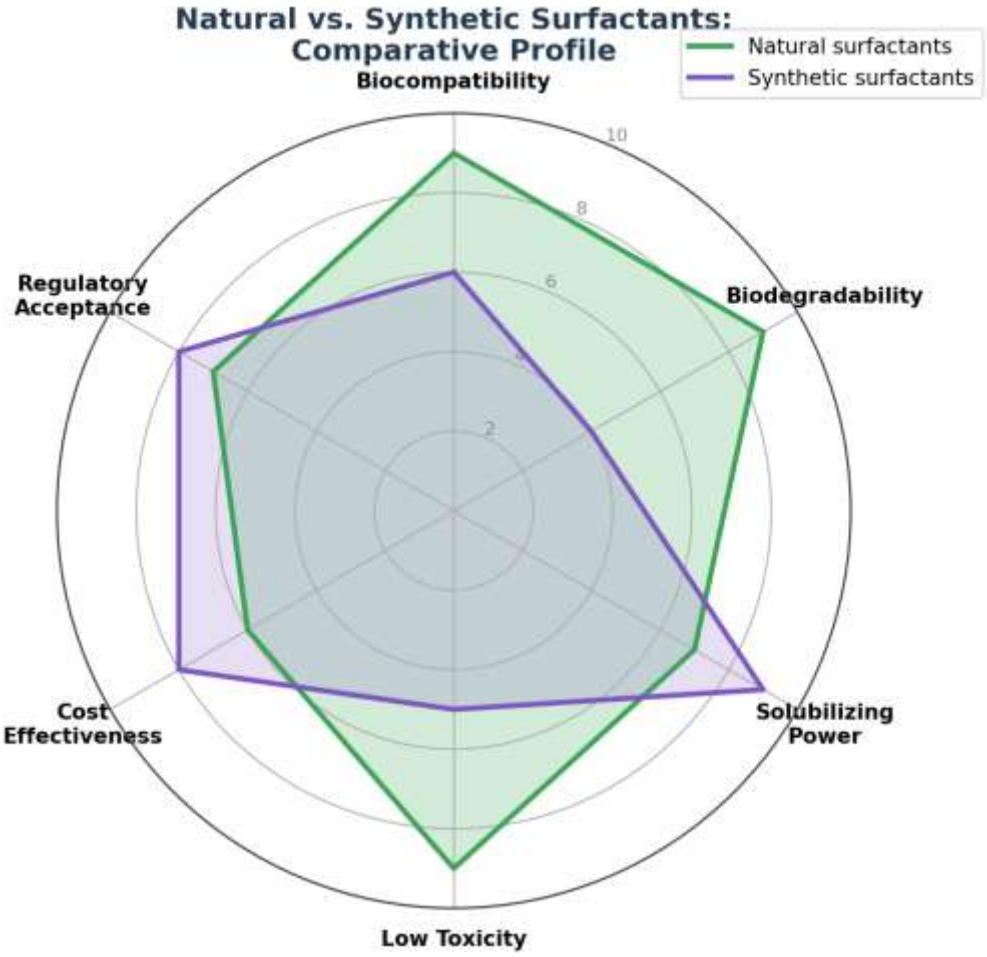

Figure 5. Comparative profile of natural versus synthetic surfactants across six pharmaceutically relevant attributes. Natural surfactants excel in biocompatibility, biodegradability and safety, while synthetic surfactants retain advantages in raw solubilising power and cost.

Natural surfactants are derived from renewable plant, animal or microbial sources and are generally biocompatible, biodegradable and of low toxicity, qualities that recommend them for pharmaceutical use (Figure 5) [16]. Lecithin, a mixture of phospholipids obtained chiefly from soybean and egg yolk, is among the most established. As a zwitterionic, food-grade emulsifier it stabilises dispersions, enhances drug solubilisation and is exceptionally well tolerated; it is frequently cited as an excellent natural surfactant option for fast-dissolving oral films, where it can be combined with soybean oil and natural polymers such as gellan gum, fenugreek mucilage and mango-peel pectin [22].

Triterpenoid and steroidal saponins constitute a second important class. These plant glycosides, widely distributed across species such as Quillaja saponaria, combine a lipophilic aglycone with one or more hydrophilic sugar chains, giving them intrinsic amphiphilicity and high surface activity. Saponins reduce surface tension, self-assemble into micelles above a critical micelle concentration of roughly 200 to 500 ppm, and can markedly enhance the permeability of biological membranes—an attribute that may further support mucosal drug absorption [15, 17]. Quillaja saponins are non-ionic, stable to heat and acidic pH, and have molecular weights in the range of 1300 to 2600 Daltons. Microbial biosurfactants such as glycolipids and lipopeptides represent a further frontier, offering tunable structures together with intrinsic antimicrobial and wound-healing activity [16].

Mechanistically, the benefit of incorporating a surfactant—whether natural or synthetic—arises from several complementary effects. By lowering interfacial tension the surfactant promotes rapid wetting of the film surface by saliva, hastening disintegration. By forming micelles it solubilises drug molecules that would otherwise dissolve only slowly, increasing the effective concentration available for absorption. And by improving the homogeneity of the casting dispersion it supports content uniformity across the film. The net result, repeatedly demonstrated in dissolution studies, is a faster and more complete release of the active relative to surfactant-free controls. The challenge for the formulator is to capture these advantages using a natural surfactant whose solubilising power, while sometimes lower than that of an aggressive synthetic such as SLS, is offset by superior safety and patient tolerability.

The selection of an appropriate surfactant is guided in part by its hydrophilic–lipophilic balance (HLB), an empirical scale that expresses the relative affinity of the molecule for water and oil phases. Surfactants with higher HLB values (above about 10) are water-soluble and favour the formation of oil-in-water systems and the solubilisation of hydrophobic drugs in aqueous media, whereas lower-HLB surfactants stabilise water-in-oil systems. Food-grade soy lecithin typically falls in an intermediate HLB range of roughly 7 to 9, while many saponins behave as effective high-HLB solubilisers. Matching the HLB of the chosen surfactant to the physicochemical requirements of the drug and the film matrix is a practical first step in rational selection. Above the critical micelle concentration, surfactant monomers spontaneously aggregate into micelles whose hydrophobic cores sequester poorly soluble drug molecules; the resulting apparent increase in solubility, sometimes by several-fold, translates directly into accelerated dissolution from the disintegrating film. For promethazine, which is already water-soluble, the surfactant's principal contributions are improved wetting, dispersion homogeneity and, where a taste-masking complex or lipophilic carrier is employed, the solubilisation of that carrier system [15, 17].

VII. MANUFACTURING TECHNIQUES

Several techniques are available for the production of oral fast dissolving films, the choice being dictated by the thermal stability of the drug, the desired throughput and the equipment available. The principal industrial and laboratory methods are solvent casting, hot-melt extrusion, semisolid casting, rolling and, more recently, printing-based approaches [20, 34].

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Figure 6. The solvent-casting workflow, the most widely used laboratory and industrial route for oral fast dissolving film manufacture, suitable for thermolabile actives such as promethazine hydrochloride.

Solvent casting is by far the most commonly employed method and the one specified in most promethazine film studies. The film-forming polymer is first dispersed or dissolved in a suitable solvent—water, ethanol or a hydroalcoholic mixture—and allowed to hydrate fully. The drug, surfactant, plasticizer, sweetener, flavour and any remaining excipients are then incorporated and the mixture is stirred to homogeneity and de-aerated to remove entrapped air bubbles that would otherwise produce defects. The resulting viscous solution is cast as a uniform layer onto an inert, non-adhesive substrate and dried under controlled temperature (typically 40 to 50 °C) to evaporate the solvent and form a coherent film. The dried sheet is finally cut into unit doses of defined area, inspected and packaged (Figure 6) [20, 32]. Solvent casting is a hydrous process well suited to both thermolabile and thermostable drugs, yields films of excellent transparency and uniformity, and offers good control over thickness and drug content—advantages that explain its dominance in research and small-scale production.

Hot-melt extrusion (HME), by contrast, is an anhydrous, solvent-free process in which the drug and polymer are blended, melted and forced through a die to form a film. It is environmentally attractive and continuous, but is restricted to thermostable drugs and polymers because of the elevated processing temperatures involved, which renders it less suitable for heat-sensitive actives. Semisolid casting, rolling methods and emerging two- and three-dimensional printing techniques—the last expected to enable on-demand, personalised dosing—complete the manufacturing landscape and point toward the future industrialisation of film products [20].

VIII. EVALUATION PARAMETERS

A comprehensive battery of tests is applied to characterise OFDFs and to confirm that they meet the required quality, performance and stability specifications. These parameters span physical, mechanical and biopharmaceutical domains [20, 31, 35].

A. Physical Properties

Thickness is measured at several points across the film using a micrometer screw gauge or calibrated digital vernier callipers; uniformity of thickness is essential because it correlates directly with the accuracy of the dose delivered. Weight variation is determined by individually weighing a sample of films and confirming that deviation from the mean falls within acceptable limits. Surface pH is assessed by placing a moistened film against a pH electrode or indicator; a value close to neutral salivary pH (around 6.8) minimises the risk of mucosal irritation. Transparency,

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appearance and homogeneity are evaluated visually, and percentage moisture content and moisture uptake are determined to predict physical stability under humid conditions, with well-formulated films typically taking up only 1 to 2% moisture [22, 31].

B. Mechanical Properties

The mechanical robustness of a film determines whether it can survive manufacture, packaging, transport and handling without damage. Tensile strength—the maximum stress a film withstands before rupture, calculated as the breaking load divided by the cross-sectional area—is measured with a texture analyser or tensile tester. Percentage elongation quantifies the film's extensibility before breaking, and the elastic (Young's) modulus describes its stiffness; hard, brittle films display high tensile strength and modulus with low elongation, whereas soft, flexible films show the reverse. Folding endurance, determined by repeatedly folding a film at the same point until it cracks (or to a defined maximum such as 300 folds), is a practical index of flexibility. As illustrated in Figure 7, both tensile strength and folding endurance generally increase with film-forming polymer concentration, while plasticizer content modulates the balance between strength and pliability [22, 31, 35].

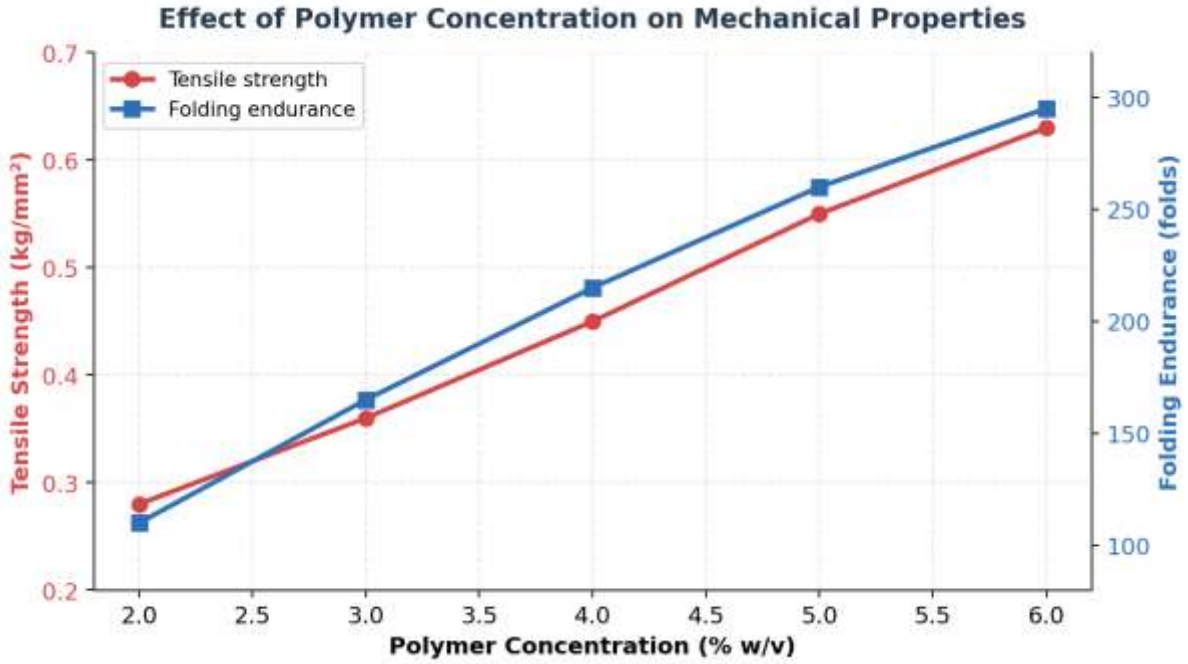

Figure 7. Illustrative relationship between film-forming polymer concentration and the mechanical properties of oral films. Tensile strength and folding endurance both rise with increasing polymer content, reflecting a denser, more cohesive matrix.

C. Disintegration and Dissolution

Disintegration time is the defining performance attribute of a fast-dissolving film. It is commonly assessed by placing the film in a small volume of water or simulated saliva and recording the time to complete disintegration, or by the petri-dish and slide-frame methods; an ideal OFDF disintegrates within a few seconds and certainly within the conventional upper limit of about 30 seconds. Reported optimised formulations frequently achieve disintegration in 9 to 20 seconds (Figure 8) [3, 31, 38]. In-vitro dissolution (drug release) is studied using a USP dissolution apparatus—typically the paddle (Type II) apparatus at 50 rpm in simulated salivary fluid—with samples withdrawn at defined intervals and assayed spectrophotometrically by UV. Optimised promethazine films and comparable antiemetic films have been reported to release in excess of 90 to 99% of their drug load within roughly 16 minutes, with surfactant-containing formulations consistently

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outperforming surfactant-free controls (Figure 9) [1, 3].

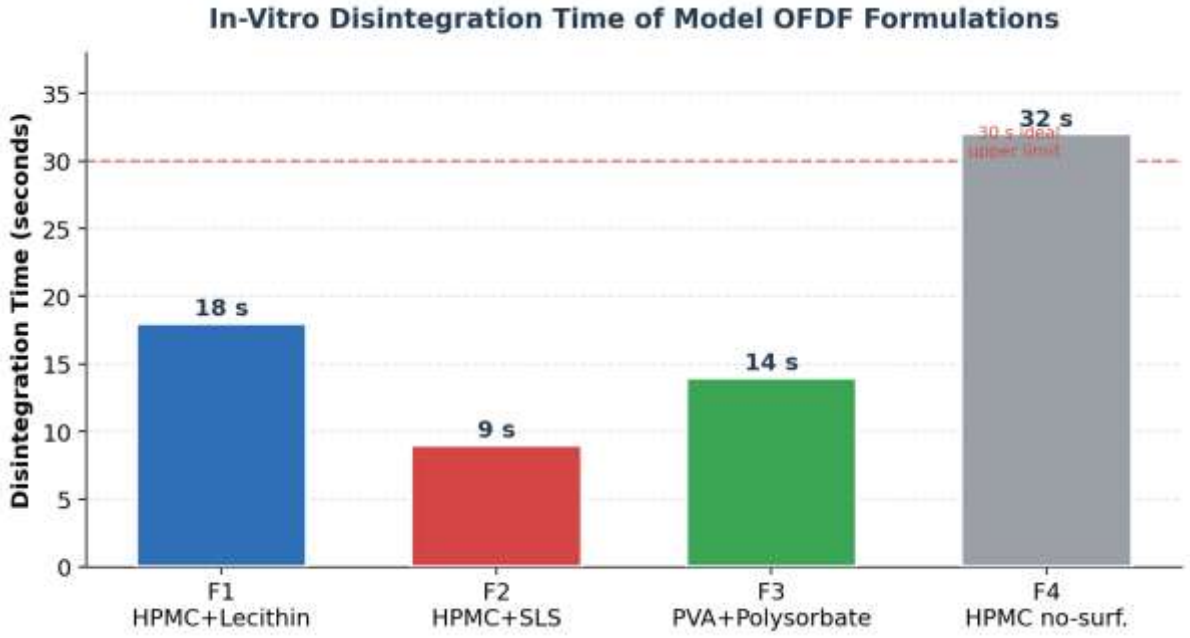

Figure 8. Illustrative in-vitro disintegration times of model OFDF formulations. Surfactant-containing films (notably HPMC + SLS, F2) disintegrate well within the 30-second ideal limit, whereas the surfactant-free control (F4) is markedly slower.

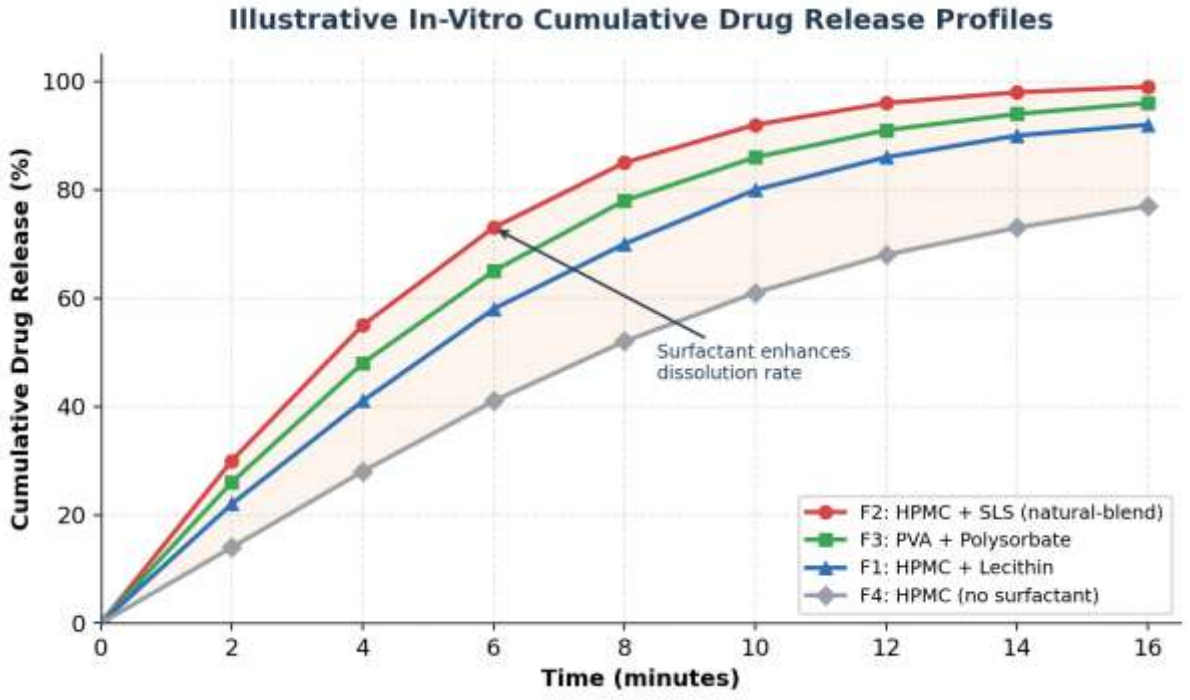

Figure 9. Illustrative in-vitro cumulative drug-release profiles of model formulations over 16 minutes. The presence of a surfactant substantially accelerates and completes drug release relative to the surfactant-free formulation (F4).

D. Drug Content, Taste and Stability

Drug content uniformity is verified by dissolving a film of known area and assaying the drug, usually by validated UV spectrophotometry or HPLC, to confirm that each unit contains the intended dose within pharmacopoeial limits. Because the film is held in the mouth, taste and mouthfeel are evaluated by trained sensory panels and, increasingly, by in-vitro bitterness assays that compare the amount of drug released into artificial saliva against the drug's bitterness threshold; an effectively taste-masked formulation releases negligible drug during the brief oral residence, as has been demonstrated for promethazine systems releasing under 1% of their load in the first minute [25]. Finally, accelerated stability studies—conducted under International Council for Harmonisation conditions, typically 40 °C and 75% relative humidity over three to six months—monitor changes in appearance, mechanical properties, disintegration time and drug content to establish shelf life [31, 35].

E. Supplementary Characterisation and Release Kinetics

Several additional tests refine the characterisation of OFDFs. The swelling index, determined by measuring the increase in film weight after immersion in a defined medium, reflects the hydration behaviour of the polymer matrix and correlates with disintegration. The contact angle of a saliva droplet on the film surface provides a quantitative index of wettability; a lower contact angle indicates more rapid wetting and is associated with faster disintegration, and it is here that surfactants exert a directly measurable effect. Surface morphology is examined by scanning electron microscopy to confirm a smooth, pore-free and homogeneous matrix, while the physical state of the drug—crystalline or amorphous—is probed by differential scanning calorimetry and X-ray diffraction; conversion of a crystalline drug to the amorphous form within the film can enhance dissolution. Drug–excipient compatibility is routinely confirmed by Fourier-transform infrared spectroscopy, which verifies the absence of adverse chemical interactions [23, 24, 36].

To interpret in-vitro release data, the dissolution profile is commonly fitted to established kinetic models. Zero-order kinetics describe a constant rate of release independent of concentration; first-order kinetics describe release proportional to the residual drug; the Higuchi model describes diffusion-controlled release from a matrix; and the Korsmeyer–Peppas power-law model, through its release exponent, distinguishes Fickian diffusion from anomalous and erosion-controlled mechanisms. For rapidly disintegrating films the release is generally fast and dominated by prompt dissolution, but kinetic modelling nonetheless provides a rigorous, comparative description of formulation performance and supports the optimisation of polymer and surfactant levels [24].

IX. RECENT ADVANCES AND COMPARATIVE STUDIES

A growing body of literature documents the formulation of promethazine and related antiemetic films, providing useful benchmarks for natural-surfactant development. Chaudhari and colleagues prepared promethazine OFDFs by solvent casting using both natural and synthetic polymers, reporting that an optimised formulation released over 99% of the drug within 16 minutes [1]. Studies employing HPMC E15 with PEG-400 and surfactants have described disintegration times as short as 9 seconds with around 96% release in 16 minutes [3]. Parallel work on taste masking has explored l-arginine-based polyamide nanocapsules, achieving release of less than 1% of promethazine into artificial saliva over ten minutes and so effectively eliminating perceptible bitterness [25], as well as Eudragit E100 solid dispersions and okra-mucilage approaches for fast-disintegrating tablets [26]. The broader OFDF field has validated natural film formers such as pullulan and natural surfactants across a range of model drugs, confirming the general feasibility of green, biocompatible film design [24, 28]. Representative findings are summarised in Table 1.

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Table 1. Representative studies on promethazine and related antiemetic fast-dissolving systems.

Study / system	Key excipients	Reported outcome
Promethazine OFDF (Chaudhari et al.)	HPMC, natural + synthetic polymers	>99% release in 16 min; rapid disintegration
Promethazine OFDF (Pathan / Ghoshi)	HPMC E15, PEG-400, SLS	~96% release in 16 min; disintegration ~9 s
Promethazine taste-masking	l-arginine polyamide nanocapsules	<1% release in artificial saliva; bitterness masked
Promethazine sublingual tablet	Eudragit E100, crospovidone	pH-dependent masking; rapid sublingual relief
Pullulan–maltodextrin OFDF (model)	Pullulan, maltodextrin (Box–Behnken)	>90% release in 5 min; disintegration ~18 s
Natural-surfactant films (general)	Lecithin, saponin, HPMC	Enhanced wetting, dissolution and tolerability

X. CHALLENGES AND FUTURE PERSPECTIVES

Despite their evident advantages, OFDFs face formulation and translational hurdles that are particularly acute for a drug such as promethazine. The limited volume of saliva and the thin geometry of the film constrain the achievable drug load, so that high-dose actives may not be deliverable in a single strip while preserving rapid, complete dissolution. The intense bitterness of promethazine demands robust taste masking that must not, in turn, retard disintegration or compromise bioavailability—a delicate balance. Maintaining the physical and chemical stability of a thin, high-surface-area film against moisture and oxidation requires careful excipient selection and protective packaging. From a manufacturing standpoint, ensuring content uniformity and reproducibility during scale-up from laboratory casting to continuous industrial production remains demanding [30, 34].

Natural surfactants introduce their own considerations: batch-to-batch variability of plant- and microbially derived materials, the need for rigorous purification and characterisation, and the sometimes lower raw solubilising capacity relative to synthetic surfactants. These are not insurmountable, and the trajectory of research is encouraging. The integration of micellar nanocarriers and biosurfactant-stabilised systems into film matrices promises to extend the range of poorly soluble drugs amenable to film delivery, while quality-by-design methodologies and statistical optimisation tools such as the Box–Behnken and factorial designs are bringing greater rigour and predictability to formulation development [24]. The anticipated commercialisation of printed, personalised films within the coming years may further transform the field, enabling on-demand dosing tailored to individual patients [18]. Continued exploration of natural surfactants sits squarely within the broader pharmaceutical movement toward sustainable, biocompatible and patient-centric excipients.

XI. CONCLUSION

Oral fast dissolving films represent a mature and rapidly growing platform that elegantly resolves the swallowing difficulties and onset limitations of conventional oral dosage forms. Promethazine hydrochloride, constrained in its conventional formulations by extensive first-pass metabolism, slow onset and pronounced bitterness, is a compelling candidate for film-based delivery, which can accelerate onset through pre-gastric mucosal absorption and improve compliance through water-free, taste-masked administration. The substitution of synthetic surfactants by natural surfactants such as lecithin and triterpenoid saponins offers a biocompatible, biodegradable and low-toxicity means of enhancing the wetting and dissolution of the active while aligning formulation practice with the demand for green pharmaceutical excipients. Drawing on the physiology of oral absorption and of the emetic reflex,

the drug's pharmacological profile, the functional roles of film-forming polymers and excipients, the dominance of solvent casting as a manufacturing route, and a comprehensive evaluation framework, this review establishes that natural-surfactant OFDFs of promethazine are both scientifically rational and commercially relevant. Realising their full potential will require continued attention to drug loading, robust taste masking, stability and reproducible scale-up, but the convergence of advances in natural excipients, nanocarrier technology and design-of-experiments optimisation provides a clear and promising path forward.

REFERENCES

[1] Chaudhari S, Patil R, Bhagwat V, et al. Formulation and evaluation of oral fast dissolving films of promethazine hydrochloride using natural and synthetic polymers. Pharm Dev Technol. 2023;28(5):738–46. doi:10.1080/10837450.2023.2211096.

[2] Ghoshi S, Dangi S. Development of fast-dissolving films of promethazine hydrochloride. Int J Pharm Sci. 2025;15(2):101–7.

[3] Pathan S, Sonawane S, Patil R, et al. Formulation and evaluation of fast dissolving films of promethazine hydrochloride. J Pharm Bioallied Sci. 2016;8(2):156–63. doi:10.4103/0975-7406.157024.

[4] Bhattacharjee A, Saha R. Oral fast dissolving films: an overview. Int J Pharm. 2017.

[5] Pahwa R, Chaudhary R. Advances in the development of oral fast dissolving films. J Control Release. 2018.

[6] Madhavi S, Joshi M. Formulation and evaluation of oral fast dissolving films of anti-emetic drugs. Asian J Pharm Sci. 2019.

[7] Shalini CM, Reddy AS, Veni VNK, Jayaprakash M, Rama Rao T. Fast dissolving oral thin films: a review. Res Rev J Drug Des Discov. 2024;11(1):24–31.

[8] National Center for Biotechnology Information. PubChem Compound Summary: Promethazine Hydrochloride, CID 6014. Bethesda (MD): National Library of Medicine; 2024.

[9] Antiemetic histamine H1 receptor blockers. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024. NBK533003.

[10] Promethazine: from first-generation antihistamine to multi-modal clinical agent – a comprehensive pharmacology review. Pharmacology Mentor; 2026.

[11] Pediatric Pharmacotherapy: Promethazine. University of Virginia Children's Hospital; 2010.

[12] Pharmacokinetics of promethazine hydrochloride. Medscape; 2009.

[13] Topical promethazine side effects: our experience and review of the literature. Biomed Res Int. 2013. PMC3852816.

[14] Promethazine – an overview. ScienceDirect Topics; Elsevier.

[15] Tan C, et al. Saponin surfactants used in drug delivery systems: a new application for natural medicine components. Int J Pharm. 2021;603:120708. doi:10.1016/j.ijpharm.2021.120708.

[16] Biosurfactants in novel drug delivery: a natural approach to enhanced therapeutics. Singapore: Springer Nature; 2025.

[17] Surface activity and emulsification properties of saponins as biosurfactants. In: Biosurfactants. Cham: Springer; 2023.

[18] Fact.MR. Oral thin film market: innovations in drug delivery systems, forecast 2024–2034. Market Research Report; 2024.

[19] Dataintelo. Pharmaceutical grade pullulan market research report 2034; 2026.

[20] Manufacturing techniques of orally dissolving films. Pharm Technol. 2024.

[21] Formulation and evaluation of fast dissolving oral film of an anti-allergic drug. Int J Pharm Sci Res. 2018.

[22] Design and evaluation of fast dissolving oral films of zolpidem by solvent casting method. Asian J Pharm Res. 2016;6(2).

[23] Rizatriptan-loaded oral fast dissolving films: design and characterizations. 2025.

[24] Development and characterizations of pullulan and maltodextrin-based oral fast-dissolving films

employing a Box–Behnken experimental design. Pharmaceutics. 2022. PMC9146677.

[25] Taste masking of promethazine hydrochloride using l-arginine polyamide-based nanocapsules. Molecules. 2023;28(2):748. doi:10.3390/molecules28020748.

[26] Taste masking of promethazine hydrochloride using Eudragit E100 via solid dispersion technique to develop fast disintegrating tablets. Int J Pharm Pharm Sci. 2010.

[27] Formulation of sublingual promethazine hydrochloride tablets for rapid relief of motion sickness. Saudi Pharm J. 2021. PMC8180616.

[28] Fast dissolving sublingual films of ondansetron hydrochloride: effect of additives on in-vitro drug release and mucosal permeation. J Adv Pharm Technol Res. 2010. PMC2964757.

[29] Formulation and evaluation of fast dissolving films for delivery of triclosan to the oral cavity. AAPS PharmSciTech. 2010. PMC2976960.

[30] Choudhary D, et al. Oral fast dissolving films: formulation strategies and natural surfactants – a review. 2025.

[31] Juber A. Development of oral fast-dissolving thin films: ingredients and applications – a review. 2023.

[32] Shruthi B, et al. Formulation and evaluation of mouth-dissolving films of an antihistamine drug. 2022.

[33] Bhattarai S, Gupta V. Fast-dissolving oral films: a novel trend in oral drug delivery. 2015.

[34] An overview of fast dissolving oral film. Int J Pharm Sci Res. 2019. ResearchGate 335853029.

[35] Oral dissolving films: a comprehensive review on recent perspectives and current approach to effective drug delivery. ResearchGate; 2022.