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DEVELOPMENT AND ASSESSMENT OF ORALLY DISSOLVING STRIPS CONTAINING METOPROLOL SUCCINATE

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ABSTRACT

Oral administration remains the preferred route due to ease of ingestion, versatility, and patient compliance, despite drawbacks such as difficulty in swallowing tablets and capsules, particularly among pediatric, geriatric, bedridden, and nauseous patients. Fast-dissolving drug delivery systems emerged in the late 1970s as an alternative to traditional oral solid-dosage forms like tablets, capsules, and syrups. These systems aim to disintegrate and dissolve quickly in the oral cavity without the need for water. Fast dissolving films, a novel drug delivery system inspired by transdermal patch technology, consist of ultra-thin oral strips applied directly onto the tongue or oral mucosal tissue. Upon contact with saliva, the film rapidly hydrates, adheres to the application site, and dissolves to release the medication for oral mucosal absorption. With formulation modifications, these films can also maintain their rapid dissolution properties for gastrointestinal absorption upon swallowing. This study aimed to formulate fast dissolving oral films of Metoprolol succinate to enhance bioavailability and circumvent presystemic metabolism. The films were developed using sodium CMC, sodium alginate, and polyvinyl alcohol polymers via the solvent casting method. Evaluation parameters included organoleptic properties, film weight, thickness, folding endurance, drug content uniformity, surface pH, disintegration time, and in vitro diffusion studies.

KEYWORDS: Dissolution test apparatus – 11 (USP-TDT08L), Cyclo-mixer, UV-Visible spectrophotometer

INTRODUCTION

Fast dissolving films represent an innovative drug delivery system designed for oral administration, drawing inspiration from transdermal patch technology. These films are applied directly onto the patient's tongue or oral mucosal tissue where they quickly absorb saliva, hydrate, and adhere. Upon application, they rapidly disintegrate and dissolve, releasing medication for absorption through the oral mucosa. With formulation adjustments, they can also maintain rapid dissolution for gastrointestinal absorption upon swallowing. This technology provides a unique product differentiation, making it suitable for expanding existing commercial product lines.

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This novel drug delivery system addresses current industry needs by enhancing drug solubility, stability, biological half-life, and bioavailability. The formulation of oral films includes various ingredients such as polymers, APIs, plasticizers, super-disintegrating agents, sweeteners, flavors, colors, saliva stimulating agents, preservatives, and surfactants. Among these, polymers, plasticizers, and super-disintegrating agents play crucial roles.

A wide range of polymers is available for formulating fast dissolving oral films, which have gained significant attention in medical and nutraceutical applications. The selection and combination of polymers are critical parameters for successful formulation development. The film must be sufficiently robust to withstand handling and transportation without damage, a quality largely influenced by the type and amount of polymer used. Typically, the film formulation should contain at least 45% w/w of polymer based on the total dry film weight, with a preference for 60 to 65% w/w to achieve desired properties.

Plasticizers are essential components in fast dissolving films as they enhance strip flexibility and reduce brittleness. They improve film forming properties by lowering the glass transition temperature

FORMULATION ASPECTS FOR ORAL DISSOLVING FILMS

Formulating oral dissolving films (ODFs) involves careful consideration of both aesthetic and performance characteristics such as taste masking, rapid dissolution, physical appearance, and mouthfeel. From a regulatory standpoint, all excipients used in these formulations must be Generally Regarded as Safe (GRAS-listed) and approved for use in oral pharmaceutical dosage forms.

A) Drug Category

ODFs are versatile in delivering various active pharmaceutical ingredients (APIs). However, due to size limitations, incorporation of high-dose drugs can be challenging. Ideally, less bitter, potent, and highly lipophilic drugs are preferred for oral thin films. Common categories of drugs used include antiemetics, neuroleptics, cardiovascular agents, analgesics, antiallergics, antiepileptics, anxiolytics, sedatives, hypnotics, diuretics, antiparkinsonism agents, antibiotics, drugs for erectile dysfunction, Alzheimer's disease, and expectorants.

B) Film Forming Polymers

Water-soluble polymers are essential as film formers due to their ability to promote rapid disintegration, good mouthfeel, and mechanical strength in the films. The robustness of the film depends largely on the type and concentration of polymer used. Several polymers are available for ODF preparation, with pullulan, gelatin, and hypromellose (HPMC) being among the most commonly used. Examples of water-soluble polymers include:

- Pullulan
- Gelatin
- Guar gum
- Xanthan gum
- Hydroxypropyl methylcellulose (HPMC)
- Modified starches
- PVPK30
- PVA

Among these, pullulan and HPMC are particularly suitable for ODFs. Pullulan, a neutral glucan similar to amylose and dextran, is produced by various strains of Aureobasidium pullulans. HPMC, a propylene glycol ether of methylcellulose, is used in low viscosity grades like HPMC E3/E5/E6/E15 for preparing medium-dispersion films.

C) Plasticizers

Plasticizers play a crucial role in ODFs by improving film flexibility and reducing brittleness. The choice of plasticizer depends on its compatibility with the polymer and the solvent used in film casting.

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3.ROLLING METHOD

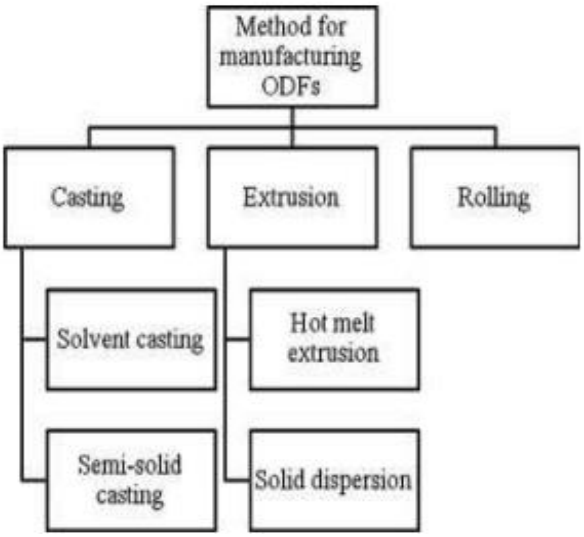

Fig.1 Method for manufacturing ODF

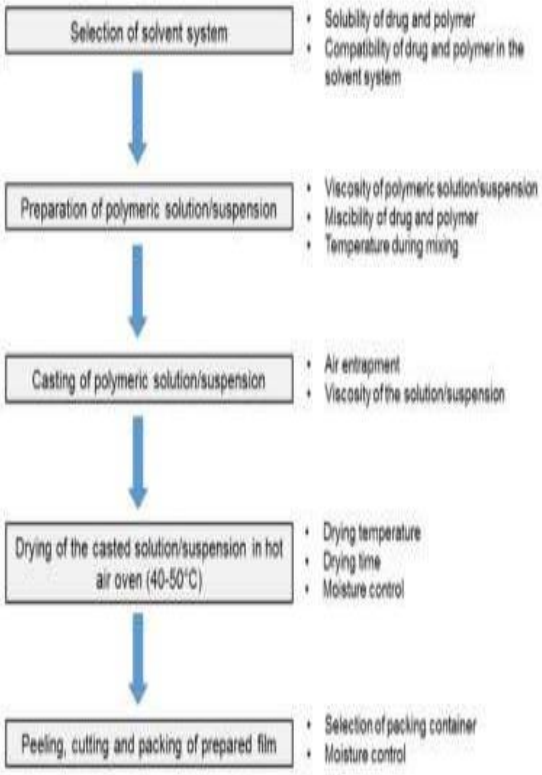

Fig. 2 Solvent casting method

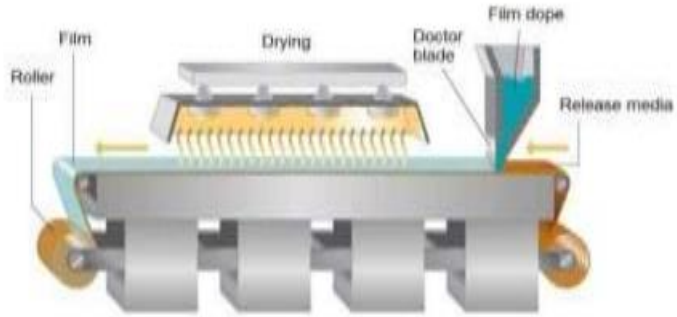

Fig.3 Hot melt extrusion

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Solubility ranges

TERMS	SOLUBILITY RANGES
Very Soluble	1 part in less than 1
Freely Soluble	1 part in l-10
Soluble	1 part in 10-30
Sparingly Soluble	1 part in 30-100
Slightly Soluble	1 part in 100-1000
Very Slightly Soluble	1 part in 1000-10000
Insoluble	1 part in more than 10000

FORMULATION OF OTF

FORMULATION CODE	F1	F2	F3	F4	F5	F6
Metaprolol succinate	100mg	100mg	100mg	100mg	100mg	100mg
Na.CMC	200mg	300mg	---	---	---	---
Na.ALG	---	---	200mg	300mg	---	---
PVA	---	---	---	---	200mg	300mg
Tween 80	q.s	q.s	q.s	q.s	q.s	q.s
Citric acid	200mg	200mg	200mg	200mg	200mg	200mg
Sodium saccharin	30mg	30mg	30mg	30mg	30mg	30mg
PEG 400	0.5ml	0.5ml	0.5ml	0.5ml	0.5ml	0.5ml
CCS	q.s	q.s	q.s	q.s	q.s	q.s
Water	q.s	q.s	q.s	q.s	q.s	q.s

CONCLUSION

Fast dissolving films of Metaprolol succinate were successfully prepared using the solvent casting method with varying concentrations of polymers PVA, NaCMC, and Na alginate (2%, 3%). The prepared films underwent comprehensive evaluation including general appearance, weight uniformity, film thickness, tackiness, folding endurance, surface pH, percent moisture loss, drug content uniformity, disintegration time, and dissolution studies, all of which met the specified limits. All formulations exhibited desirable characteristics of flexibility, smoothness, non-stickiness, and transparency without visible particulate matter. The surface pH ranged between 6.6 to 7.75, indicating close proximity to neutral pH, which is ideal for oral formulations. Among the six formulations tested, those containing sodium CMC and PVA polymers demonstrated rapid drug release compared to formulations containing sodium alginate.

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