RESEARCH ARTICLE

Design of Mouth Dissolving Polyherbal Films for Dental Caries

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ABSTRACT

Oral disease is still a major public health problem across the globe in developed countries as well as developing countries. Dental caries is one of humans' oldest and most prevalent diseases or conditions of factor situations. The present study was designed to evaluate the antimicrobial potential of polyherbal film containing extracts of *Annona squamosa* L*, Mentha piperita* and *Acalypha indica* leaves against *Streptococcus mutans.* The mouth-dissolving poly herbal films were formulated with 1% (OF1), 2% (OF2) and 3% (OF3) extract concentrations. OF3 produced better results than OF1 and OF2 in folding endurance, disintegration time and dissolution time. The antimicrobial properties of the polyherbal films and standard marketed formulations S1 and S2 mouthwash were evaluated against the dental pathogen, *S. mutans*. OF3 produced a zone of inhibition 18.3 ± 0.21 mm compared to S2 which produced an inhibition zone of 27.0 ± 0.24 mm, whereas S1 has not shown any zone of inhibition. These results indicated that the mouth dissolving poly herbal films could be effective in the treatment of dental caries and gingivitis.

Keywords: Polyherbal film, Mouth dissolving, Dental caries, Dental pathogen, *Streptococcus mutans.*

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INTRODUCTION

Good dental or oral care plays an important role in maintaining healthy teeth and gums. The unhygienic mouth may contain bacteria such as *Streptococcus mutans, S. sobrinus* and *Lactobacillus casei* which can damage teeth and gums.[1] These bacteria get adhered to the teeth, form a plaque, and develop film around it which gets attached to the surface of the enamel. These bacterial plaques lead to oral ailments such as dental decay and gingivitis. *S mutans* is a gram-positive, cocci shaped bacterium that gets attached to the enamel surface and synthesize an extracellular polysaccharide matrix in presence of sugars like sucrose, fructose, and glucose which leads to the formation of caries in dental cavities after 6 to 24 months.[2,3] According to a review of epidemiological data nearly 5000 million people across the globe suffer from dental caries. Sugar is the main cause of dental caries, whereas dietary acids present in items such as soft drinks play a major role in dental erosion.[4] Dental diseases substantially impact self-esteem, nutrition and health despite a low mortality rate.[5]

A wide variety of oral care products are available in the market, including toothpaste, mouth rinses, dental floss, saliva substitutes, and mouth spray. Using toothpaste by brushing technique is difficult for paediatric and geriatric patients and sometimes unacceptable due to its taste. Mouthwash is one of the consumer-friendly oral hygiene products but is associated with a risk of swallowing the mouth wash accidentally which cannot be avoided in the case of small children. Some oral cleansers contain alcohol and may result in drying of the mouth and can also stain the tooth if used for a prolonged period. Gel preparations have to be applied with gentle care but cannot be reached to all sites of mouth.[6] To overcome these difficulties an approach was made to prepare a convenient mouth dissolving poly herbal film, and these films get dissolved within a quick period in the mouth without chewing or drinking water or. A novel oral fast-dissolving films offers simple administration method with the convenience of dosing without water.[7]

Annona squamosa L, *Mentha piperita,* and *Acalypa indica* have been reported in the literature to be useful in relieving toothache, gingivitis, and gum bleeding disorders.[8] Based on their reported utility in oral care, the above plants were selected to formulate mouth dissolving herbal films and evaluate their antimicrobial potency against *S. mutans*.

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MATERIALS AND METHODS

Plant Material

Leaves of *A. squamosa* L*, M. piperita, and A. indica* were collected from surroundings of Bangalore on 25th August 2019, authenticated by Dr. N. M Ganesh Babu, Centre for Herbal Gardens, TDU Bengaluru. A voucher specimen (AS- 234, MP-235, AI-236) has been kept in Pharmacognosy Department for future reference. *S. mutans MTCC 890* was procured from MTTC, Chandigarh, Punjab. Mitis salivarius agar media was procured from Hi media Laboratories.

Preparation of Extracts

The leaves from the plants *A. squamosa* L*, M. piperita* and *A. indica* were collected dried under shade and powdered. The powdered drugs were extracted with 95% ethanol using soxhlet apparatus. Extraction was carried out for 48 hours, then concentrated, and then dried in a desiccator.[9]

Phytochemical Screening

Alcoholic extracts of the leaves were subjected to phytochemical screening for the detection of primary and secondary metabolites.[10]

Pre-formulation Studies

Based on the literature survey, blank films were prepared using several polymers such as HPMC E5, PEG 400, PEG 200, sodium alginate, ethyl cellulose, pectin, and polyvinyl pyrrolidone K30 in various concentrations and ratios.[11] The parameters used for the selection of the final polymers and their ratios were the ability of film formation, flexibility, drying rate, disintegration time, and folding endurance.

Antimicrobial Screening of the Extracts

The plant extracts were mixed in the ratio 1:1:1 to prepare polyherbal extract and screened for its antimicrobial property by agar diffusion method.[12] Mitis salivarius agar media was prepared and sterilized by autoclaving at 121°C for 20 minutes. The sterile media was poured into sterile petri plates to a thickness of approximately 4 mm and allowed to solidify. Bores were created in the media using a sterile borer and the plates were uniformly seeded with *S. mutans* suspension using sterile swab. The different concentration of polyherbal extract was then incorporated into the bores and incubated at 37°C for 24 hours. The antimicrobial screening was initially carried out for 0.5% of the polyherbal extract, followed by testing using 1, 2 and 3% mixture.

Preparation of Poly Herbal Oral Films

Polyherbal films were prepared according to the formulation given in Table 1. Weighed quantity of HPMC E5 and required quantity of PEG 400 were added into a beaker with 5 g of ethanol with through mixing. Weighed quantity of sodium benzoate, aspartame and polyvinyl pyrrolidone was dissolved in minute quantity of distilled water. The prepared solutions were mixed homogeneously to obtain a clear solution and incorporated with polyherbal extract. Glycerol 0.5 mL and 0.02 g peppermint oil were added, then the final weight was made up to 10 g. Polymeric mixture (6 g) containing extracts was casted into a 7 cm diameter petri plate and dried at 50°C.

Table 1: Selected formulation for polyherbal film

Ingredients	*OF1*	*OF2*	*OF3*
Poly herbal Extract* (%)	1	2	3
HPMC E5 (g)	1.3	1.3	1.3
PEG 400 (g)	0.1	0.1	0.1
Polyvinyl Pyrrolidone K30 (g)	0.004	0.004	0.004
Aspartame (g)	0.02	0.02	0.02
Na Benzoate (g)	0.01	0.01	0.01
Glycerol (mL)	0.5	0.5	0.5
Peppermint oil (g)	0.02	0.02	0.02
Ethanol (g)	5	5	5
Water	q.s	q.s	q.s
Total weight (g)	10	10	10

Evaluation of Polyherbal Films[13-15]

Organoleptic characters

Film color uniformity was evaluated visually, while the intensity of the flavoring agent determined odor and surface texture and feel or touch, respectively.

Physico–mechanical Properties

Weight variation

Determined by weighing the film sections of 1-cm^2 size, which were prepared by cutting at five different places.

Thickness

The thickness of the patch was determined by the microscopic method. Two coverslips were placed together in a vertical position, the thickness was measured (F1), and a film was placed in between the coverslips to measure the thickness (F2). The difference between F2 and F1 gave the film thickness.

Folding endurance

Determined by repeated folding of the film at the same place until the film breaks. The number of times the film is folded without breaking was considered.

Disintegration time

Films of 1-cm^2 were used to determine the disintegration time.

Table 2: Standards used for antimicrobial activity comparison

Sl. No.	*Marketed formulation*	*Composition*
1	S1	Menthol 0.042%, thymol 0.064%, methyl salicylate 0.06%
2	S2	Chlorhexidine gluconate 1.0% w/w Flavoured base

Table 3: Percentage yield and nature of the extract

Sl.No	*Extract*	*Colour*	*Consistency*	*Percentage yield (%)*
1	*A. squamosa*	Reddish-brown	Semi-solid	31.36
2	*M. piperita*	Greenish-brown	Solid	22.86
3	*A. indica*	Black	Semi-solid	30.16

Table 4: Zone of inhibition of extracts

Microbial strain	*S. mutans MTCC 890*					
Solvent	DMSO			Alcohol		
Code	D1	D2	D3	A1	A2	A3
Concentration (%)	1	2	3	1	2	3
Zone of Inhibition (mm)	23.0 ± 0.05	23.0 ± 0.08	25.0 ± 0.07	20.0 ± 0.03	21.0 ± 0.07	21.0 ± 0.07

Mouth Dissolving Time

Preparation of simulated saliva fluid (6.8 pH)

Simulated saliva, pH 6.8 was prepared as per the standard procedure and the mouth dissolving time was determined by placing the film (1-cm^2) into a beaker containing 50 mL of prepared simulated saliva fluid.

Antimicrobial studies of the polyherbal film

Antimicrobial studies of the polyherbal film against *S. mutans* were carried out by agar diffusion method.[12] The zone of inhibition for the standard marketed gel, mouthwash and the polyherbal films was measured. Two marketed standards S1 and S2 were used for comparison and their composition are shown in Table 2.

RESULTS AND DISCUSSION

Alcohol extracts of *A. squamosa* L, *M. piperita* and *A. indica* leaves were prepared by soxhlet extraction method. The percentage yield and nature of the extract are shown in Table 3.

Phytochemical Screening

All the three extracts were found to contain alkaloids, glycosides, tannins, phenolic compounds and flavonoids. Plants with above bioactive constituents were found to posses' significant antimicrobial activity.[16]

Pre-formulation Studies

Pre-formulation studies with different polymers in varying concentrations and ratios were carried out. The formulation prepared using HPMC E5 (1.3 g), PEG 400, polyvinyl pyrrolidone K30, and 0.5 mL glycerol was found to be non-sticky, smooth, and transparent. The folding endurance of the film was good and the disintegration time was found to be less than 1.5 minutes. Hence, this proportion was further used to develop films incorporated with different concentrations of extracts.

Antimicrobial Screening of Extracts

The polyherbal extract was prepared by combining the extracts in the ratio 1:1:1. Antimicrobial studies of the polyherbal extracts (0.5, 1, 2, and 3%) were carried out by agar diffusion method against a representative strain of oral bacteria, *S. mutans*. 0.5% polyherbal extract showed negative results with no zone of inhibition. The zone of inhibition of 1, 2 and 3% polyherbal extract is tabulated in Table 4 and the zone of inhibition is shown in Figure 1. Since 1, 2, and 3% polyherbal extract showed inhibitory activity against *S. mutans*, these concentrations were further selected for the formulation of polyherbal films.

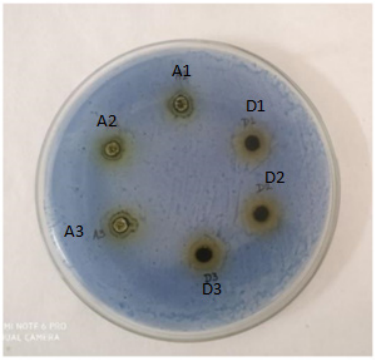

Figure 1: Antimicrobial activity of the polyherbal extract

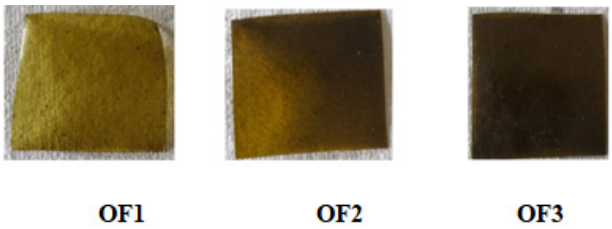

Figure 2: Polyherbal mouth dissolving films

Preparation of Polyherbal Films

Sections of polyherbal films prepared with three different concentrations of extracts are shown in Figure 2.

Evaluation of the Mouth Dissolving Polyherbal Oral Film

The films prepared with 1, 2, and 3% of extracts were evaluated for its organoleptic and physico-mechanical properties and the results are summarized in Tables 5 and 6.

The green color in the films intensified with the increase in the percentage of extract. The odor was pleasant and aromatic. All films had a smooth feel and texture. Weight variation test showed uniformity of weight at different sections of the film. The thickness ranged from 59.85 ± 0.39 to 63.84 ± 0.47 mg. There was no significant increase in thickness due to the incorporation of a higher concentration of extracts. The folding endurance ranged from 150 ± 0.50 to 169 ± 0.57. OF3 showed the highest flexibility in terms of folding endurance values. The disintegration time and mouth dissolving time decreased with increasing extract percentage in the films. OF3 was found to exhibit the least disintegration time and mouth dissolving time of 45 ± 0.76 and 32 ± 0.51 seconds, respectively.

Antimicrobial Studies of Polyherbal Films

Antimicrobial studies of the polyherbal films were carried out by the agar diffusion method against *S. mutans* using mitis salivarius media. The zone of inhibition for the standard

Table 5: Organoleptic evaluation parameters

Parameters	*OF-1*	*OF-2*	*OF-3*
Color	Light green	Green	Green
Odor	Aromatic	Aromatic	Aromatic
Surface texture	Smooth	Smooth	Smooth

Table 6: Physico-mechanical evaluation parameters

Parameters	*OF1*	*OF2*	*OF3*
Weight variation(mg)	0.0236 ± 0.08	0.0275 ± 0.05	0.0259 ± 0.05
Thickness (µm)	59.85 ± 0.39	63.84 ± 0.47	61.18 ± 0.40
Folding endurance	169 ± 0.57	150 ± 0.50	172 ± 0.81
Disintegration time (sec)	72 ± 0.82	58 ± 0.58	45 ± 0.76
Mouth dissolving time (sec)	41 ± 0.70	35 ± 0.42	32 ± 0.51

Table 7: Zone of inhibition of films

Microorganism	*Zone of inhibition (mm)*				
	S1	*S2*	*OF1*	*OF2*	*OF3*
S. mutans MTCC 890	27.0 ± 0.24	No zone	15.0 ± 0.45	16.5 ± 0.19	18.3 ± 0.21

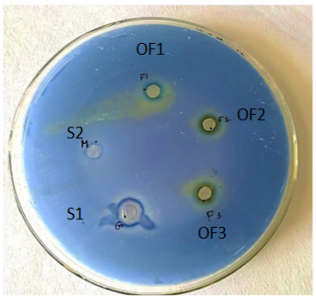

Figure 3: Antimicrobial activity of polyherbal films

marketed gel, mouthwash, and polyherbal films was measured and the results are shown in Table 7 and Figure 3.

The films containing 3% extract exhibited the highest inhibition zone of 18.3 ± 0.21 mm when compared to 1 and 2%. The zone of inhibition was compared with the marketed standard formulation. S1 exhibited no zone of inhibition, while S2 produced a zone of 27.0 ± 0.24 mm and marketed mouthwash containing essential oils in its composition was considered a better comparative standard for the formulated polyherbal films.

CONCLUSION

The prepared mouth-dissolving polyherbal films exhibited rapid dissolution with favorable physical-mechanical properties. The results of the study proved that the mouth-dissolving poly herbal films could be effective in maintaining oral hygiene, thus offering protection against dental caries and gingivitis.

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