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RESEARCH ARTICLE

FORMULATION AND CHARACTERIZATION OF ORODISPERSIBLE FILMS OF *SOLANUM XANTHOCARPUM*

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ABSTRACT

Solanum xanthocarpum belongs to the family Solanaceae commonly known as the Indian night shade or Yellow berried night shade (English) and kantakari (Sanskrit). *Solanum xanthocarpum* has played an important role in the traditional medicine. The aim of present invention is to formulate and develop ODFs of hydro-alcoholic extract of *Solanum xanthocarpum*. ODFs of *Solanum xanthocarpum* extract were prepared using solvent casting method. The percentage yield of Hydroalcoholic extract of *Solanum xanthocarpum* was found to 3.35 % by using maceration method under laboratory conditions. The results of phytochemical screening show the presences of various bioactive compounds such as Carbohydrates, Flavonoids, Proteins & Amino acids, Diterpenes and Saponins. Phenol s or phenolic compounds were found to absent in Hydroalcoholic extract *Solanum xanthocarpum* roots. Among the prepared formulations, formulation F1 was found to have transparent visual appearance, best film forming capacity, least disintegration time and also found to be stable at accelerated stability studies. Evaluation of the films confirmed their potential as an innovative dosage form to deliver *Solanum xanthocarpum.*

Key words: *Solanum xanthocarpum,* phytochemical test and oral dissolving films (ODF).

INTRODUCTION:

From past one decade, there has been an enhanced demand for more patient-friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increased greatly. Oral dissolving films (ODF) are the latest development in this field. ODFs are the ultrathin films of postage stamp size with an active agent or active pharmaceutical ingredient and other excipient (Grigoli, 2010). These dosage forms can rapidly disintegrate and/ or dissolve to release the medicament as soon as they come in contact with saliva thus obviating the need for water during administration, an attribute that makes them highly attractive for pediatric and geriatric patients (Shukla et al., 2009). ODFs provide accurate dosing in safe and efficacious format, without the need of measuring devices as is the case with liquid oral dosage forms.

Solanum xanthocarpum (SX) Schrad. & Wendl. (Family: Solanaceae) commonly known as the Indian night shade or Yellow berried night shade (English) and kantakari (Sanskrit). It is a prickly diffuse, bright green perennial herb, woody at the base, 2–3 m height, found throughout India, mostly in dry places as a weed along roadsides and waste lands. SX has held a place of some importance in the Hindu Materia Medica, primarily as an expectorant and antipyretic. Various medicinal properties are attributed to it, particularly in the treatment of asthma, chronic cough and catarrhal fever. It is one of the members of the dashamula (ten roots) of the Ayurveda (Mohan *et al*., 2007). Chemical examinations of berries of SX were initially done by Saiyed and Kanga, (1936). Which led to the isolation of glycoalkaloid, solasonine. From the non alkaloidal portion, a glycoside of β-sitosterol with galactose as a sugar moiety has been obtained along with two phenolic substances, which could be identified as methyl caffeate and caffeic acid (Saiyed and Kanga, 1936).

Development of herbal medicines in novel drug delivery systems is the need of hour. This approach is an interesting blend of therapeutic effectiveness of herbal medicines and advantages of novel drug delivery systems. This increases the patient compliance for the useful herbal drugs, which generally are free from side effects. At present, researchers are working toward developing novel drug delivery systems such as mouth-dissolving tablets, soft gelatin capsules, sustained and extended release formulations, Mucoadhesive systems, transdermal dosage forms, micro particles, microcapsules, nanoparticles, implants, etc. of herbs, along with this, many oral retention formulations consisting of gels, pastes, and chewing gums have been developed from the last few years. But poor flow ability, poor compressibility of plant extracts, requirement of more functional excipient, etc. poses formulation hurdles for the development of such novel formulations (Devi *et al*., 2010). But as recent market studies indicate that among the different oral marketed dosage forms, ODFs are largely gaining acceptance as the delivery system of choice. Thus there is a great need to deliver this potentially useful herbal drug into the ODF.

The aim of present invention is to formulate and develop ODFs of hydro-alcoholic extract of *Solanum xanthocarpum*. The ODFs were formulated using wide range of film-forming agents such as hydroxypropyl methylcellulose (HPMC), Pullulan, maltodextrin, polyvinyl alcohol (PVA). The polymers were used alone and in combination to obtain the desired film

properties which were later evaluated for film forming properties, physico-mechanical properties, palatability, microbial limit test, accelerated stability studies, and clinical efficacy test. HPMC is known for its good film-forming properties and has excellent acceptability. Maltodextrin is classified as a complex carbohydrate, but acts such as a simple carbohydrate in the body. It acts as film-forming agent, solubilizer, and imparts sweetness to the formulation. Pullulan is natural water-soluble polysaccharide, produced from starch by fermentation. It is an excellent film-former. For the fabrication of films, polyethylene glycol (PEG) 4000 was used as a plasticizer along with preservative, sweetener, emulsifier, flavoring agent.

MATERIAL AND METHOD

Collection of plant materials

The leaves of *Solanum xanthocarpum* were collected from Vindhya Herbals, Bhopal in the month of April 2022

Authentication of Plant Materials

Authentication of collected plant materials were confirmed by Expert Botanist, from Barkatullaha University, Bhopal, Madhya Pradesh, India.

Extraction (By Maceration Method) (Pandey et al., 2014)

Collected plant drugs namely *Solanum xanthocarpum* leaves were cleaned properly and washed with distilled water to remove any kind of dust particles. Cleaned and dried plant drugs were converted into moderately coarse powder in hand grinder. Powdered plant drugs were weighed (60 gm) and packed in (1 liter) air tight glass Bottle. The plant drugs were subjected to extraction by Methanol and water (20:80) as solvent for about 24 hrs. The liquid extracts were collected in a tarred conical flask. The solvent removed from the extract by evaporation method using hot plate. The extracts obtained with each solvent were weighed to a constant weight and percentage w/w basis was calculated.

Preliminary Phytochemical Screening

Preliminary phytochemical screening means to investigate the plant material in terms of its active constituents. In order to detect the various constituents, present in the Hydroalcoholic extract of leaves of *Solanum xanthocarpum*, were subjected to the phytochemical tests as per standard methods (Kokate, 1994; Harborne, 1976).

Preparation of *Solanum xanthocarpum* ODFs

ODFs of *Solanum xanthocarpum* extract were prepared using solvent casting method. The formulation codes and their respective compositions are given in Table 1. *Solanum xanthocarpum* extract was mixed with measured amount of water using over headed stirrer for 5 min. The extract was then filtered through the muslin cloth. To this filtered extract of *Solanum xanthocarpum*, successively measured amounts of polymer, tween 80, bronopol, sweetening and flavoring agents were added, and the solution was stirred for 30 min. The thick viscous solution was degassed to remove air entraps by ultrasonication.

Table 1: Composition of different formulation of ODFs of *Solanum xanthocarpum*

Ingredients	F1	F2	F3	F4	F5	F6	F7
Solanum xanthocarpum extract	10	10	10	10	10	10	10
HPMC 5cps	30	-	-	-	15	15	15
Maltodextrin	-	30	-	-	15	-	-
Pullulan	-	-	30	-	-	15	-
PVA	-	-	-	30	-	-	15
Polyethylene glycol	10	10	10	10	10	10	10
Polysorbate 80	5	5	5	5	5	5	5
Bronopol	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Sucralose	3	3	3	3	3	3	3
Distilled water	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S

Note: quantities given in mg/film, HPMC: Hydroxypropyl methylcellulose, PVA: Polyvinyl alcohol

Measured quantity of solution was casted on a 30 × 45 cm^2 glass plate and was kept in hot air oven at about 80°C for 15 min. The film was carefully removed from the glass plate,

checked for any imperfections and cut to the required size to deliver the dose equivalent to 100 mg (2 × 3 cm^2) per film. The films were stored in airtight plastic containers for further studies. The film samples were also stored for accelerated stability studies as per International Conference on Harmonization (ICH) guidelines.

EVALUATION METHODS

Preliminary characteristics

Film forming capacity: It is the ability of a polymer to form films that can be separated from the surface on which they are casted. The films were characterized as very poor, poor, average, good, better, best depending upon their ability to form films (Dixit et al., 2009).

Appearance of films

Appearance of film was evaluated by visual observation. The films were characterized as transparent or translucent (Patel et al., 2009; Tingstad, 1964).

Tackiness

Upon stacking the films should not stick to each other. This is a criterion which a film should possess for better dispensing of dosage form.

Thickness

All the formulations were evaluated for uniformity in thickness by using calibrated digital vernier caliper. Ten films (pieces) from each formulation were taken randomly from different places of the plate. Thickness was measured and means value was calculated. The uniformity in thickness is directly related to the accuracy of dose in the film (Dixit et al., 2009; Patel et al., 2009).

Folding endurance

The folding endurance was measured manually for the prepared films. A film was cut and firmly folded through the middle. The number of folds on the same crease, required to produce crack in the film was noted as the value of folding endurance (Dzija et al., 2003; Shinde et al., 2003).

Surface pH study

The surface pH of fast dissolving strip was determined in order to investigate the possibility of any side effects in vivo. As an acidic or alkaline pH may cause irritation to the oral mucosa, it was determined to keep the surface pH to neutral as close as possible. A combined pH electrode was used for this purpose. Oral strip was slightly wet with the help of water. The pH was measured by bringing the electrode in contact with the

surface of the oral film. The experiments were performed in triplicate, and average values were reported.

Disintegration test

Disintegration test was performed in the USP disintegration apparatus. Simulated salivary fluid (PH 6.8) was used as the medium. The films were placed in the tubes of the container and the discs were placed over it. The average disintegration time of six films from each formulation was noted.

Organoleptic evaluation

Since the ODFs are intended to disintegrate rapidly in oral cavity, the product needs to have accepted organoleptic palatable characteristics. Organoleptic evaluation of prepared ODFs was carried out on panel of healthy volunteers with sound organoleptic senses, with their prior consents. The ODFs were rated on the basis of taste, mouth feel (grittiness or smoothness) and physical appearance. Table 2 gives the key for the organoleptic evaluation of ODFs.

Table 2: Key for evaluation of Organoleptic study

Parameters	Taste	After taste	Physical appearance
0	Not good	Not bitter	Not good
+	Good	Slightly bitter	Good
++	Very good	Bitter	Very good
+++	Excellent	Very bitter	Excellent

Stability studies

For stability testing the ODFs were stored under controlled conditions of 40°C±2°C/75%±5% RH, 30°C±2°C/75%±5% RH over a period of 3 months according to the ICH guidelines. During storage the ODFs were checked for their physical appearance, tackiness and disintegration time.

RESULTS AND DISCUSSION

The plant drug (20g) was subjected to extraction by (maceration) using Hydroalcohol as solvent for about 24 hrs. The liquid extracts were collected in a tarred conical flask. The solvent removed from the extract by evaporation method using hot plate. The extracts obtained with each solvent were weighed to a constant weight and percentage w/w basis was calculated. The yields were

found to be (3.35 % w/w of crude drug) of Hydroalcoholic extract *Solanum xanthocarpum* leaves. Obtained results were recorded in table 3.

The results of Preliminary Phytochemical Screening of Hydroalcoholic extract of *Solanum xanthocarpum shows the presence of* Carbohydrates, Flavonoids, Proteins & Amino acids, Diterpenes and Saponins. Phenol s or phenolic compounds were found to absent in Hydroalcoholic extract of *Solanum xanthocarpum*. The results of phytochemical revels that the all polar and Methanolic and aqueous soluble compound was found to be present in *Solanum xanthocarpum* extract. Table 4.

Table 3: Extractive values obtained from *Solanum xanthocarpum*

S.N.	Solvent	% Yield
1.	Methanol+water (20:80)	3.35%

Table 4: Preliminary phytochemical screening of *Solanum xanthocarpum*

S.N.	Phytoconstituents	Test Name	Hydroalcoholic Extract
1	Alkaloids	Wagner's Test	**+(ve)**
2	Carbohydrates	Fehling's Test	**-(ve)**
3	Flavonoids	Lead acetate	**+(ve)**
		Alkaline reagent test	**+(ve)**
4	Proteins & Amino acids	Precipitation test	**+(ve)**
5	Phenols	Ferric chloride test	**-(ve)**
6	Diterpenes	Copper acetate test	**+(ve)**
7	Saponins	Foam test	**+(ve)**

Observations of film

Preliminary Characteristics

Determination of film forming capacity, visual appearance and tackiness for all the formulations are shown in Table 5. Pullulan alone and in combination with HPMC exhibited poor film forming capacity. Pullulan otherwise is good film forming agent but film forming ability of formulation F3 was found to be poor.

The reason may be the presence of *Solanum xanthocarpum* extract that interferes in the linking of Pullulan molecules and hence structure flexibility of the films is not achieved. The higher temperatures involved in drying may also cause changes in the mechanical properties of the films, making them brittle and less flexible films. Similarly, F6 also did not result in good films.

This indicated that in this ratio of HPMC and Pullulan the films could not be formed. The reason can be incompatibility between two polymers or the interference of drug extract with the films. Rest of the formulations showed good film forming abilities. F4 also yielded films with average quality. It explained the nature of PVA when used alone as film forming agent. Visual appearance of all films was found to be transparent and free of air bubbles, which is necessary for aesthetic appeal.

All the formulations were found to be non-tacky at ambient conditions except ODFs containing Pullulan. This might be because of slightly hygroscopic nature of Pullulan. So the formulations F3, F4, and F6 were not studied further as they failed at the first stage only.

Thickness

The thickness of all films was found to be in the range of 0.05-0.07 mm (Table 6). The difference in the thickness of these formulations might be due to the different viscosities of the polymers which were used to formulate the films. The low standard deviation values for the thickness of these formulations were confirming efficiency of the method that was employed for formulation of films.

Table 5: Evaluation of Film forming properties of different polymers with *Solanum xanthocarpum*

Formulation code	Film forming capacity	Appearance of films	Tackiness
F1	Very good	Transparent	Non tacky
F2	Very good	Transparent	Non tacky
F3	Poor	Transparent	Slightly tacky
F4	Average	Transparent	Non tacky
F5	Very good	Transparent	Non tacky

F6	Poor	Translucent	Non tacky
F7	Very good	Transparent	Non tacky

Table 6: Evaluation of physical properties of *Solanum xanthocarpum*

Formulation code	Film thickness (mm)	Disintegration (s)	Surface pH	Folding endurance
F1	0.07±0.23	22±0.22	6.90±0.84	258±0.56
F2	0.05±0.27	8±0.41	7±0.21	298±0.25
F5	0.06±0.53	16±0.70	7.1±0.30	351±0.46
F7	0.07±0.41	61±0.30	6.81±0.61	193±0.84

Folding endurance

All the polymers were able to give the acceptable folding endurance values. Figure 1 shows the results for all the formulations, the observed folding endurance was in the order F5 > F6 > F2 > F1.

Folding endurance was found to be highest for formulation F5 (351±0.46). Combination of maltodextrin and HPMC 5 cps was found to perform better the folding endurance was increased.

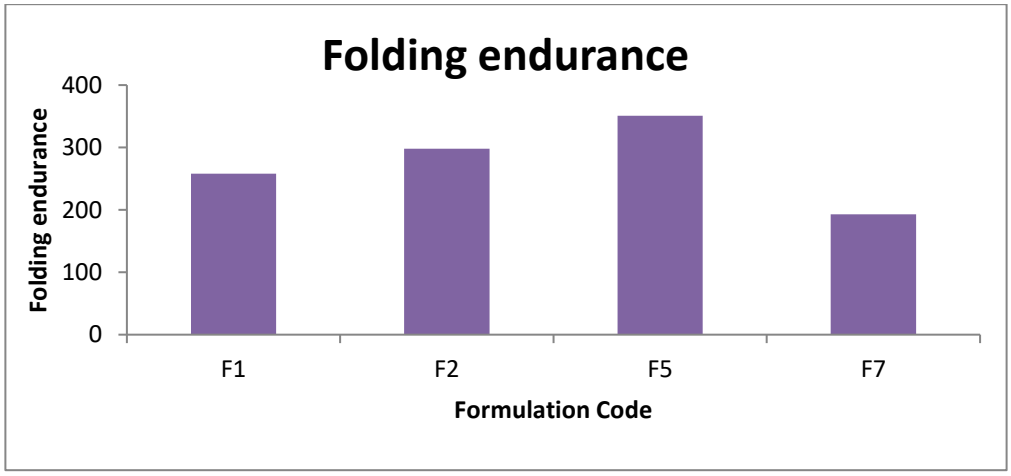

Figure 1: Comparative study of folding endurance of ODFs of *Solanum xanthocarpum*

Surface pH study

The surface pH values of the formulations are given in Table 6. All the polymers resulted in the formulations that have neutral surface pH. The surface pH of the strips was ranging from 7.1±0.30 to 6.90±0.84. The neutral values of surface pH of films assured that there will not be any kind of irritation to the mucosal lining of the oral cavity.

In vitro disintegration time

All the films were found to be rapidly disintegrating except F7 (Table 6, Figure 2). The observed disintegration time was in the order F2 > F5 > F1 > F7 as show in Figure 6.2. PVA was found to increase the disintegration time of HPMC films. It must be because of the slow solubility of PVA in water that delayed solubility of HPMC. Quickly disintegrating character of maltodextrin was retained even in the presence of other ingredients of film thus allowing F2 to disintegrate rapidly (disintegration time 8±0.41s). Presence of maltodextrin reduced the disintegration time of HPMC from 24 to 17 s.

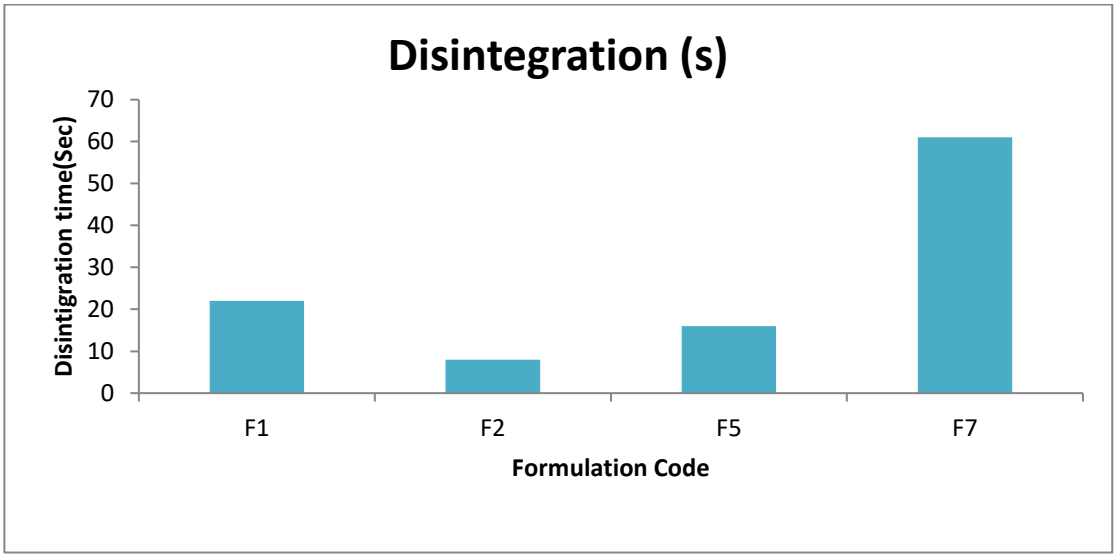

Figure 2: Comparative study of disintegration time of ODFs of *Solanum xanthocarpum*

Organoleptic evaluation

The results of the organoleptic characterization are shown in Table 7. All the formulations scored well in physical appearance but formulations F2 and F5 were found to be excellent in palatibity test. This suggested that maltodextrin acts both as film-forming agent and sweetener thus enhances palatability of formulation F2 and F5. All the formulations also showed no bitter after taste, except F7. It suggested that appropriate amounts of flavors and sweeteners have already been incorporated in the

films. The failure of F7 in after taste parameter might be due to the higher disintegration times required which ultimately reduces the palatability of prepared films. Formulation F7 was discarded at this stage and was not studied further.

Table 7: Organoleptic characterization of selected formulations

Formulation code	Taste	Bitter aftertaste	Physical appearance
F1	++	0	+++
F2	+++	0	+++
F5	+++	0	+++
F7	0	+	+++

Accelerated stability studies

The results of accelerated stability studies are given in Table 8. When selected *Solanum xanthocarpum* ODFs formulations were stored at 40±2°C and 75%±5% RH, 30±2°C and 75%±5% RH changes were observed in formulation F2 and F5 in physical appearance, tackiness, separation of the films. The formulation F1 was found to be stable and subjected to the disintegration test. The formulations F2 and F5 were found to be tacky and difficult to separate at accelerated stability conditions because of very hygroscopic nature of maltodextrin at relative humidities greater than 50%.

Table 8: Stability studies of selected formulations

Formulation code	Physical appearance	Tackiness	Film separation	Disintegration time (s)	
				40±2°C, 75%±5% RH	30±2°C, 75%±5% RH
F1	Very good	Non tacky	Separates	24±0.34	23±0.95
F2	Good	Tacky	Difficult to separate	NA	NA
F5	Good	Tacky	Difficult to separate	NA	NA

CONCLUSION

The presence of bioactive compounds such as alkaloids and flavonoids in the Hydroalcoholic extract of *Solanum xanthocarpum* have large no of medicinal values. Among the prepared formulations, formulation F1 was found to have transparent visual appearance, best filmforming capacity, least disintegration time and also found to be stable at accelerated stability studies. Evaluation of the films confirmed their potential as an innovative dosage form to deliver *Solanum xanthocarpum*. Thus, *Solanum xanthocarpum* ODFs are found to be suitable especially for geriatric, bedridden, and non-cooperative patients due to its ease of administration as well as patient friendly dosage form.

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