FORMULATION AND EVALUATION OF SERTRALINE HYDROCHLORIDE ORAL DISPERSIBLE FILMS USING NATURAL POLYMERS

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Abstract

One often prescribed antidepressant is sertraline hydrochloride. It is a selective serotonin reuptake inhibitor (SSRI) approved to treat major depressive disorder, social anxiety disorder, and a variety of other psychiatric problems. Due to the first-pass effect, sertraline hydrochloridehas low bioavailability and limited water solubility. In order to eliminate the limitations ofsertraline hydrochloride, this work intends to create sertraline hydrochlorideoral dispersible films (ODF) utilizing the solvent casting process.The films are able to be eaten without water, making formulation for pediatric, geriatric, and dysphagic patients easier. Due to their inexpensive cost and lack of adverse effects, the natural polymers like sodium alginate, pullulan, and xanthan gumwere used to create the oral dispersible films.Formulations were made using polymers in different amounts ranging from F1 to F12. All of the formulations underwent physical evaluations for their weight, thickness, folding endurance, tensile strength, drug content, surface pH,*in-vivo* drug dissolution profile within pharmacopeial limitations. In comparison to the other formulations, the F3 formulation, which contains 50 mg of sodium alginate, released the medication cumulatively at a rate of 97.83% in 5 minutes.

Keywords: Sertraline HCL, Oral dispersible films,Sodium alginate, Pullulan andxanthan gum

I. INTRODUCTION

The goal of a scientist or dosage form designer is always to increase a drug's safety while preserving its therapeutic efficacy. Recent developments in novel drug delivery systems (NDDS) work toward this goal by creating an easy-to-use dose form to increase patient compliance. The fastest dissolving drug delivery system has been developed by pharmaceutical technologists[1]. Typically, a pill is made to be chewed or swallowed whole in order to provide patients with a precise amount of medication. However, some patients especially those who are young or elderly

have trouble swallowing or chewing solid dose forms. Oral dispersible films were created to help these patients.The films are able to be eaten without water, making formulation for pediatric, geriatric, and dysphagic patient's easier[2].The minimal amount of saliva required for these formulations typically results in film breakdown in the oral cavity. The medication can then be taken as a solution to be absorbed from the gastrointestinal tract, or it can be absorbed completely or partially into the systemic circulation from blood vessels in the oral mucosa.When compared to orally consumed tablets, oral mucosal route typically results in a quicker beginning of action, and the part absorbed through the blood vessels avoids the hepatic first-pass metabolic processes[3].An antidepressant of the selective serotonin reuptake inhibitor (SSRI) class, sertraline hydrochloride is also known as ((1S, 4S)-4-(3, 4-Dichlorophenyl)-1, 2, 3, and 4-Tetrahydro-N-methyl-1- naphthalenamine hydrochloride).The suppression of serotonin (5HT) uptake by CNS neurons is thought to be sertraline's primary mode of action[4]. The use of sertraline is permitted for the treatment of a number of conditions, including depression, obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), premenstrual dysphoric disorder (PMDD), panic disorder (PD), social phobia/social anxiety disorder, genernal anxiety disorder, binge eating disorder, and premature ejaculation. Sertraline has a significant first-pass metabolism 44% in oral availability. Sertraline hydrochloride is making it a good choice for oral fast-releasing systems. Thereforein the present investigation of oral dispersible films was developed by using natural polymers like sodium alginate, pullulan, and xanthan gum with different concentrations.

II.MATERIALS AND METHODS

Sertraline hydrochloride was obtained as a gift sample from KP Labs, Hyd. Sodium alginate, pullulan, and xanthum gum were purchased from Nihal PVT.ltd., Hyd and remaining materials were analytical graded.

2.1. Preparation of sertraline hydrochloride films: Sodium alginate, pullulan and xanthan gum were used as film formers. PEG 400 as plasticizer, aspartame as sweetening agents and the films were prepared by solvent casting method. Film forming polymers were dissolved in 20 ml of hot water and stirred vigorously to obtain a clear solution (solution I). Sertraline hydrochloride was dissolved in 10 ml distilled water containing plasticizer (solution II). Then solution I and solution II were mixed and the final solution was allowed to stand overnight at room temperature to remove the air bubbles. Then, 7 ml of the solution was poured into a petri dish. The petri dishes were kept in vacuum desiccator until completely dried. The films were then carefully removed and examined for any imperfection. The resulting films were cut into squares with dimension of 2.5×2.5 cm^2. In this way, each square contained 25 mg of the active ingredient[6,7,8]. The composition of the final formulations is illustrated in Table 1.

Table 1: Formulae of sertraline hydrochloride oral dispersible films using natural polymers

S.No	Ingredients (mg/ml per film)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Sertraline Hydrochloride	25	25	25	25	25	25	25	25	25	25	25	25
2	Sodium alginate	40	45	50	55	-	-	-	-	-	-	-	-
3	Pullulan	-	-	-	-	40	45	50	55	-	-	-	-
4	Xanthan gum	-	-	-	-	-	-	-	-	40	45	50	55
5	Propylene glycol-400	8	10	12	12	8	10	12	14	8	10	12	14
6	Citric Acid	3	3	5	5	3	3	5	5	3	3	5	5
7	Aspartame	4	5	6	6	4	5	6	6	4	5	6	6
8	Tween -80	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8
9	Flavour	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
10	Distilled water	30	30	30	30	30	30	30	30	30	30	30	30

2.2. Determination of weight and thickness:10 films' weight variation was measured using a digital balance (Shimadzu, Japan). Each sample's thickness was determined using a verniercaliper and the mean thickness was computed[9,10].

2.3. Determination of tensile strength of films:A texture analyzer (model CT3, Brookfield, USA) with a 1-kg load cell was used to assess the mechanical qualities of films. Film strips of a constant size (5 cm x 1 cm), free of air bubbles or other physical flaws were clamped between two clamps spaced 4 cm apart. The upper clamp tugged the strips at a speed of 0.2 mm/s during the measurement. The film was broken, and the force and elongation were recorded. Each formulation's measurements were carried out three times. Tensile strength (TS) and the percentage of elongation were determined as two mechanical properties for the evaluation of the films[11].

2.4. Taste masking studies: The film formulations with the best physical properties were chosen. Volunteers assessed the effectiveness of sweetening and flavouring ingredients in reducing

sertraline hydrochloridebitter taste. The masking effectiveness of sweetening and flavouring additives was evaluated by 18 healthy adult volunteers, who gave the formulations a weak (-), fair (), good (+), and very good (++) rating[12,13] .

2.5. Drug content uniformity: To create a homogenous solution, one piece of 2.5 cm^2 of the film with a nominal amount of 25mg setraline hydrochloride was dissolved in 100 ml of simulated saliva pH 6.8 (phosphate buffer with NaCl) for 30 minutes while being continuously shaken. Then, 10 ml of this solution was diluted to 50 ml using fake saliva. Utilizing a UV Spectrophotometer, the absorbance was measured at 310 nm (Shimadzu, Japan).The experiment was carried out three times for the films of all compositions[14].

2.6. *In-vitro* dissolution studies: *In-vitro* dissolution study of fast dissolving films of setraline hydrochloride was performed using USP type II (paddle apparatus) in 500 ml simulated salivary fluid (pH 6.8). Dissolution media was kept at 37.5±0.5°C and paddle rotating rate was set to 100 rpm. Every 30 sec, 5 ml of samples were withdrawn, and replaced with the same amount of fresh medium. UV absorbance of samples was read at 310nm and the percentage of drug released was plotted against time[15-17].

III.RESULTS AND DISCUSSION

3.1.Preparation of sertraline hydrochloride oral dispersible films: Oral dispersible film formulation different formulations were created using variable concentrations of pullulan, xanthan gum, sodium alginate, and aspartame. Oral films that dissolve quickly should have a high water solubility to quickly release their material.The formulations were chosen for future investigations based on the criteria of film-forming ability, elasticity, flexibility, and detachability from the surface, disintegrating time and taste masking ability.The disintegrating time profile and taste masking ability were given in Table 2 and 3.

Table 2:The ability of sweetening agents employed in formulations to disguise tastes

S.No	Formulation	Sweetening agent
1	F1	-
2	F2	
3	F3	++
4	F4	+
5	F5	-
6	F6	
7	F7	++
8	F8	+
9	F9	-
10	F10	
11	F11	+
12	F12	++

3.2. Characterization of oral dispersible films: The outcomes of the physical characterization of the films are shown in Table 4. As indicated by the data, the thickness and medication content of the chosen formulations were both consistent. The findings of the study of surface pH demonstrated that formulations' pH levels were close to neutral. This demonstrates that the likelihood of irritating the oral mucosa is relatively low. Formulations with a folding endurance of more than 300 that they were resilient and adaptable. To assess the tensile strength and elasticity of films, tensile testing was utilised. Tensile strength (TS) and elongation at break (E/B) were two parameters that were defined. Pullulan and sodium alginate were the main components of F3 and F7, which had higher tensile strength and E/B. A weak and soft polymer typically exhibits low TS and E/B, whereas a strong and brittle polymer exhibits high TS and low E/B. In fact, a hard tough polymer exhibits a high TS and E/B while a soft tough polymer exhibits a moderate TS and high E/B. As a result, formulations F3 and F7 are durable and effective.

Table 3: The disintegrating time profile of sertraline hydrochloride oral dispersible films F1-F12

S.No	Formulation	Disintegration time(sec)
1	F1	44
2	F2	46
3	F3	50
4	F4	51
5	F5	42
6	F6	50
7	F7	52
8	F8	50
9	F9	51
10	F10	52
11	F11	55
12	F12	53

Table 4: Physical characteristics of sertraline hydrochloride oral dispersible films F3, F7 and F12

Formulation	Drug content (%)	Thickness(mm)	Folding endurance	Surface pH	Weight variation(mg)	Tensile strength(g/cm$^{2)}$
F1	92.34±0.21	0.32±0.02	273	6.90±0.01	63.12±1.34	56.12±4.05
F2	96.17±0.01	0.34±0.01	281	6.92±0.03	62.45±2.32	58.35±3.02
F3	99.09±0.17	0.39±0.01	301	7.01±0.04	65.86±2.87	62.23±1.06
F4	95.67±0.34	0.35±0.01	309	6.99±0.02	67.91±3.24	63.05±0.05

F5	91.23±0.21	0.33±0.02	282	7.02±0.03	69.23±1.23	61.23±2.02
F6	95.87±0.78	0.34 ±0.03	294	6.99±0.01	69.67±9.68	66.07±5.02
F7	98.63±0.09	0.44±0.01	307	7.05±0.06	70.56±2.72	68.02±0.45
F8	94.78±0.52	0.31±0.02	310	7.03±0.03	70.12±2.31	68.03±2.12
F9	93.04±0.43	0.32±0.04	261	6.89±0.01	64.56±4.12	53.12±2.02
F10	95.02±0.56	0.35±0.01	273	6.90±0.04	65±23±3.10	55.03±4.01
F11	97.10±0.12	0.40±0.03	284	7.07±0.02	67.46±2.09	57.00±0.56
F12	97.89±0.04	0.45±0.01	300	7.10±0.08	66.72±2.03	60.32±0.12

3.3. *In vitro* dissolution tests: USP type II (paddle apparatus) *in vitro* drug dissolution investigations of all formulations showed that formulations F3, F7 and F12 dissolved drug in maximum percentage than other formulations 97.83%, 91.5% and 85.6% respectively with 5mins. The drug dissolution profiles demonstrate rapid dissolving and hence quick drug release for all film formulations.Fig.1, 2 and 3 were demonstrated that drug dissolution profile all formulation (F1-F12) with three different natural polymers in different proportions. These film formulations quickly dissolve, leading to quick drug release.

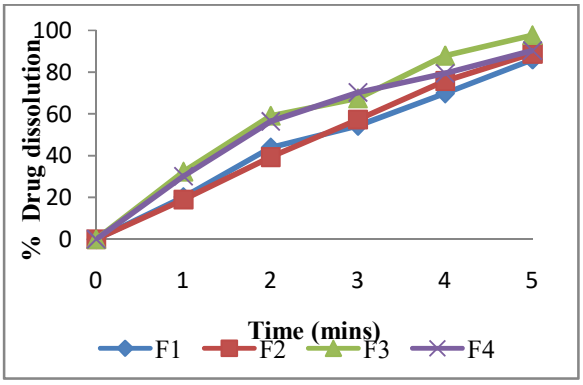

Fig.1. *In vitro* drug dissolution profile of sertraline hydrochloride films using sodium alginate (F1-F4)

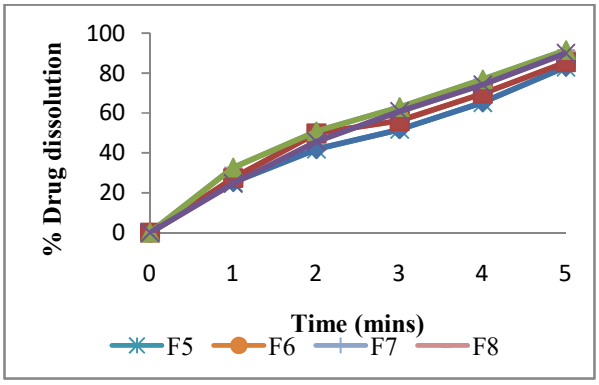

Fig.2. *In vitro* drug dissolution profile of sertraline hydrochloride films using pullulan (F5-F9)

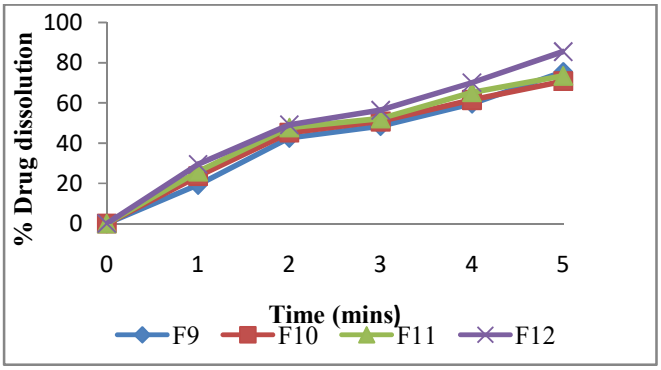

Fig.3. *In vitro* drug dissolution profile of sertraline hydrochloride films using xanthan gum (F9-F12)

IV.CONCLUSION

The present research investigation utilizes the natural polymers such as sodium alginate, pullulan, and xanthan gum as film formers with varying ratios, as well as PEG 400 as plasticizers were used in the development of oral dispersible films containing sertraline hydrochloride. All the ODFs were displayed the proper physical properties, including in vitro dissolution profile, flexibility, acceptable surface pH, folding endurance, tensile strength, and thickness.In comparison to the other formulations, the F3 formulation, which contains 50 mg of sodium alginate, dissolved the medication at a rate of 97.83% in 5 minutes. Therefore oral dispersible films appear to be a good replacement for the commercially available oral dose form of sertralin hydrochloride, offering better patient compliance, greater bioavailability, and quicker action at a lower cost with the help of natural polymers.

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