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Research

Development And Assessment Of Oral Disintegrating Films Made Of Dexlansoprazole Utilizing Natural Polymers

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Abstract

The medication's efficacy and safety profile may be enhanced, dosage may be decreased, and the onset of action may be accelerated with oral disintegrating films. Compared to other conventional dose forms, it dissolves more quickly, remains more stable, and has a longer half-life. Dexlansoprazole (DXP) was used for the sublingual route in order to produce fast-dissolving films that dissolves in saliva quickly and without the need for water. DXP ODFs were designed to improve bioavailability and patient compliance. In order to assist the aged, bedridden, and mentally ill, the recipes were developed. The influence on the dissolution profile is measured using DXP. The solvent casting method was used to create the oral disintegrating films (ODFs), which contained PEG 400 as an active ingredient and plasticiser along with natural polymers including guar gum and chitosan in different proportions. The results showed that the medicine vanished quickly. According to this study, DXP might be administered orally using an oral disintegrating film. ODF formulations release all of the drug in 20 minutes after dissolving smoothly and readily. There was no particle matter or residue left after disintegration. It was found that the solvent casting technique worked well for creating the rapidly dissolving DXP films. Oral disintegrating films (ODF) have been used successfully with patients who are immobile, schizophrenic, or travelling when there is no access to water. Prepared films showed a faster start of action and a higher rate of dissolution, which resulted in better patient compliance, effective treatment, and future use growth.

Keywords: Dexlansoprazole, solvent casting technique, guar gum, chitosan, oral disintegrating films.

INTRODUCTION

Orally disintegrating tablets and Oro dissolving films are two of the fast-dissolving medication delivery technologies that have been developed as alternatives to traditional dose forms in order to help these individuals. Because oral medicine delivery has the highest compliance rate, especially among pediatric and geriatric patients, it is considered the most practical, affordable, and safest drug delivery method. Any medication delivery system's ultimate purpose is to successfully deliver the drug to the body. Among the different dosage forms, the oral disintegrating dosage form is the most popular commercial product[1]. The film decreases the risk of choking and the fear of choking, is simple to make, easy to handle and administer, and has handy packaging. It also lessens the taste that is unpleasant. These thin polymer films are also known as melt-in-mouth dosage forms (MDF), mouth dissolving films (ODF), quick dissolving films (QDF), rapidly dissolving films (RDF), and oral dissolving films (ODF)[2].

Some formulations were developed earlier that are atorvastatin[3], zolmitriptan[4], levocetrizine dihydrocloride[5], amlodipine besylate[6], ondansetron[7], promethazine hydrochloride[8], risperidone[9].

Dexlansoprazole is white to almost white crystalline powder that is freely soluble in ethanol, methanol, dichloromethane, dimethyl formamide, ethyl acetate, and acetonitrile; they are nearly insoluble in hexane, hardly soluble in ether, and barely soluble in water. It used to treat "heartburn" or erosive esophagitis brought on by gastroesophageal reflux disorder (GERD)[10].

Natural polysaccharide chitosan is odourless yellowish powder, frequently utilized in orodispersible medication delivery systems for several reasons, such as biocompatibility, Mucoadhesive property, promotes absorption[11]. Guar gum is a powder that ranges from off-white to yellowish-white. Five to eight times the thickening capacity of starch. Aqueous solutions are devoid of taste, odorless, non-toxic, exhibit a mild transparent gray color and possess a neutral pH. It serves as a suspending, thickening, stabilizing, and tablet binder and disintegrant in the pharmaceutical industry[12]. To be best of our knowledge ODFs of DXP with natural polymers chitosan and guar gum were not found in the literature. The present research aims to develop oral disintegrating films that contain the drug Dexlansoprazole, which is proton pump inhibitor used in the treatment of gastro-oesophageal reflux disease (GERD).

MATERIALS & METHODS

Chemicals

Dexlansoprazole was obtained as gift sample from UniChem laboratories Ltd., Hyderabad. Chitosan was obtained from Sain Medicaments Pvt Ltd., Hyderabad. Guar gum SLN Chemicals, Hyderabad. PEG purchased from Merck lifescience Pvt Ltd., Hyderabad. Citric acid from S.D Fine chemical, Mumbai, India. Sod. Saccharine was purchased from Himedia Lab Pvt Ltd., Hyderabad. Orange flavour was purchased from Elite Flavours, Hyderabad. All the chemicals or excipients used were of analytical grade.

Construction of calibration curve of DXP by UV spectrophotometry[13]

A 100 millilitre volumetric flask is filled with 100 milligrammes of carefully weighed DXP. The volume was raised to 100 ml using 6.8 pH phosphate buffer, and this is the stock solution of 1 mg/ml. Using 6.8 pH phosphate buffer, the stock solution was further diluted (0.5, 1, 1.5, 2, 2.5, and 3 ml were taken from stock solution and diluted with 100 ml buffer) to create solutions with concentrations of 5, 10, 15, 20, 25, and 30 µg/ml. A UV-VIS spectrometer (EI 1372, Electronics India, Pune, India) was used to plot a standard graph and measure the absorbance of these solutions at a wavelength of 284 nm. A blank of 6.8 pH phosphate buffer was employed for this purpose.

Drug - Polymer Compatibility Studies (FTIR)

An FTIR study was carried out to ascertain whether the drug and polymers were compatible. The infrared spectra of DXP were recognised using the ATR FTIR spectrometer (Bruker Alpha II FTIR Spectrometer, Mumbai, India). The mid-IR 8000-400 cm-1 spectral range was covered by the diffuse reflectance approach. The process entails utilizing a motor to disperse the sample in KBr (100 mg), then a compression gauge to triturate the materials into a fine powder bed inside the holder. For five minutes, the pressure was about five tons. The pellet was positioned along the light path, the spectrum was captured twice, and the distinctive peaks of the functional groups were deciphered.

Formulation Design[14]

Using the solvent casting method, DXP ODFs were made with natural polymers called chitosan and guar gum. We set a formula with the following components:

Table 1: Formulation of Dexlansoprazole ODF

Ingredients	DF 1	DF 2	DF 3	DF 4	DF 5	DF 6	DF 7	DF 8
Dexlansoprazole (Dose of 30 mg per film)	750	750	750	750	750	750	750	750
Chitosan (%w/v)	2	2.5	3	3.5	--	--	--	--
Guar gum (%w/v)	--	--	--		0.5	1	1.5	2
PEG 400 (%w/v of polymer wt.)	10	10	10	10	10	10	10	10
Sod. Saccharine (%w/v)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Orange Flavor	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S

*The above formulation was calculated for 25 films of 2x2 cm size.

Preparation of ODF

We employed the solvent casting method to make Dexlansoprazole ODF. The ODF of DXP was made using the natural polymers guar gum and chitosan. After dissolving chitosan in 70 millilitres of 1% v/v acetic acid, guar gum was added and mixed until it was completely dissolved. To enable the polymer to swell, the polymeric solution was thereafter allowed for five to six hours. After dissolving DXP in 30 millilitres of water, the drug solution was incorporated to the previously discussed polymeric solution. Additionally, orange flavour, plasticiser (PEG 400), and sod. saccharin were added. A cyclo mixer was used to mix the entire solution for 15 to 20 minutes. The solution is stirred in a magnetic stirrer for two hours to break up any trapped air bubbles, and then it is set aside. The solution is then poured onto a square glass plate (10 cm x 10 cm x 1.7 cm, Othmro, Amazon, India) and allowed to air dry for the entire night in order to form a film. Following drying, the film was carefully removed from the mould, examined for defects, and cut to the right size to ensure that each strip had the right dosage (2×2 cm2). The study did not include film samples with cuts, air bubbles, or other defects.

Evaluation of oral disintegrating films formulations

Thickness measurement[15]

The film's thickness was measured five times using a micrometer screw gauge, and an average of three readings was determined.

Weight variation[16]

Using an analytical balance, the average weight of the mouths dissolving the oral films was calculated for each film.

Folding endurance[17]

The value of folding endurance is determined by the number of times the film could be folded in the same way without breaking.

Drug content uniformity

By evaluating the API content in each individual strip, content consistency is ascertained. 85–115% is the maximum content homogeneity[18].

Surface pH

The film that was going to be tested was put in a Petri dish, wet with 0.5 milliliters of distilled water, and left for thirty seconds. After allowing one minute for equilibration and contacting the formulation's surface with the pH meter's electrode, the pH was recorded. For every formulation, an average of three determinations was made[19].

Assay of the Films

The drug content of the prepared Oro dissolving films was tested. One film, chosen at random from the five, was weighed, then added to 100 milliliters of 6.8 pH buffer in a volumetric flask. For thirty minutes, a volumetric flask was submerged in a sonicator. The finished solution's absorbance was measured at 284 nm utilizing a UV Visible spectrophotometer against a 6.8 pH buffer blank. Concentrations and formulation amount were calculated using a standard graph.

Tensile strength[20]

The greatest stress applied to the point at which the strip specimen breaks is known as its tensile strength.

***In vivo* disintegration studies**[21]

Disintegration test equipment was used. Disintegration time indicates film disintegration and decomposition. In a stainless steel wire mesh with 25 ml of pH 6.8 simulated salivary fluids, place the desired film size (2x2 cm2). The time it takes the film to dissolve is called disintegration time.

***In vitro* Dissolution test**[22]

An in-vitro dissolving analysis of the created ODF formulations was conducted using EI -1916, Electronics India, Pune, India; USP type I dissolution test instrument (basket). Drug concentration was determined

using the standard graph and reported as a percentage of the drug that was released or dissolved. The release studies were conducted in six duplicates, and mean values were noted.

Release Kinetics[23]

The findings from the invitro diffusion investigation were used to investigate the order and mechanism of drug release kinetics of DXP films. The kinetic models that were plotted included the zero order, first order, and Higuchi equations; the release was calculated using the Korsmeyer-Peppas equations.

Stability Studies

The designated formulations were tagged and placed in strip packing with aluminium foil in polyethylene packets. After that, they were kept at 40°C/75% RH. Maintained for three months and assessed, in accordance with ICH Guidelines, for their outward look, medication content, and drug release at predetermined intervals[24].

RESULTS & DISCUSSION

DXP's calibration profile

The stock solution is made by combining 50 mg of DXP with 100 ml of water. After removing 10 millilitres of this stock solution, 100 millilitres were created by diluting it with water. With the appropriate stock solution dilution and a range of concentrations (2–10 µg/ml), a calibration curve was produced. We measured the absorbance at 284 nm. In Figure 1, the DXP standard curve is shown. In a pH phosphate buffer with a pH of 6.8, DXP was calibrated; linearity was found with 0.9885 R^2 value.

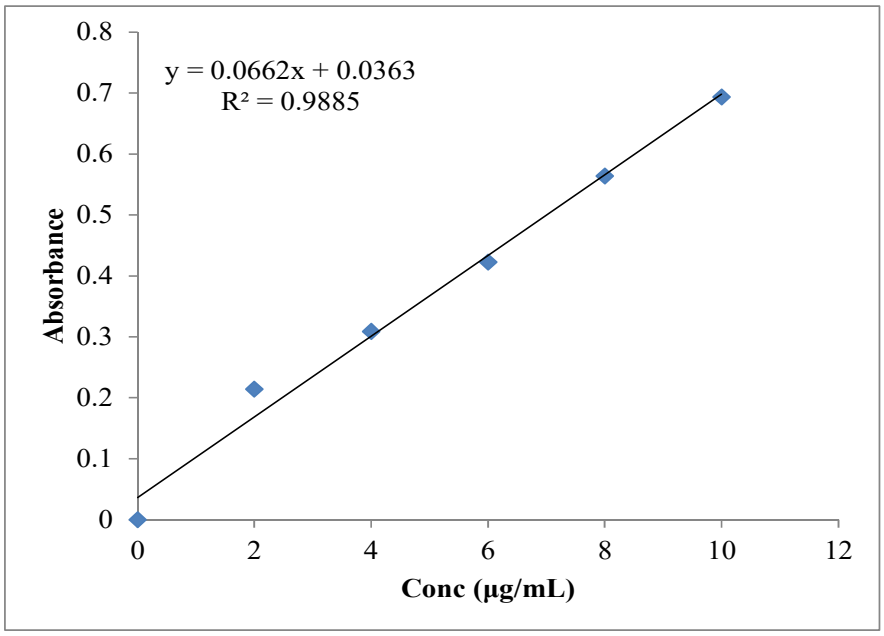

Fig 1: Standard Calibration Curve of DXP

Drug – excipient Compatibility Studies

FTIR spectroscopy was used to determine the drug excipient compatibility, and the graphs from the figure were displayed. To find out if there was any interaction between the excipients and DXP, the physical mixture was put through FTIR analysis. The lack of a drug-carrier chemical interaction is confirmed by the absence of any drug-characteristic peak appearance or disappearance. DXP, chitosan and guar gum physical mixtures all had their Fourier transform infrared spectra recorded and examined for chemical interactions. All samples, which were pure DXP, underwent FTIR analysis to determine the presence of the pure API in the mixtures and to describe it.

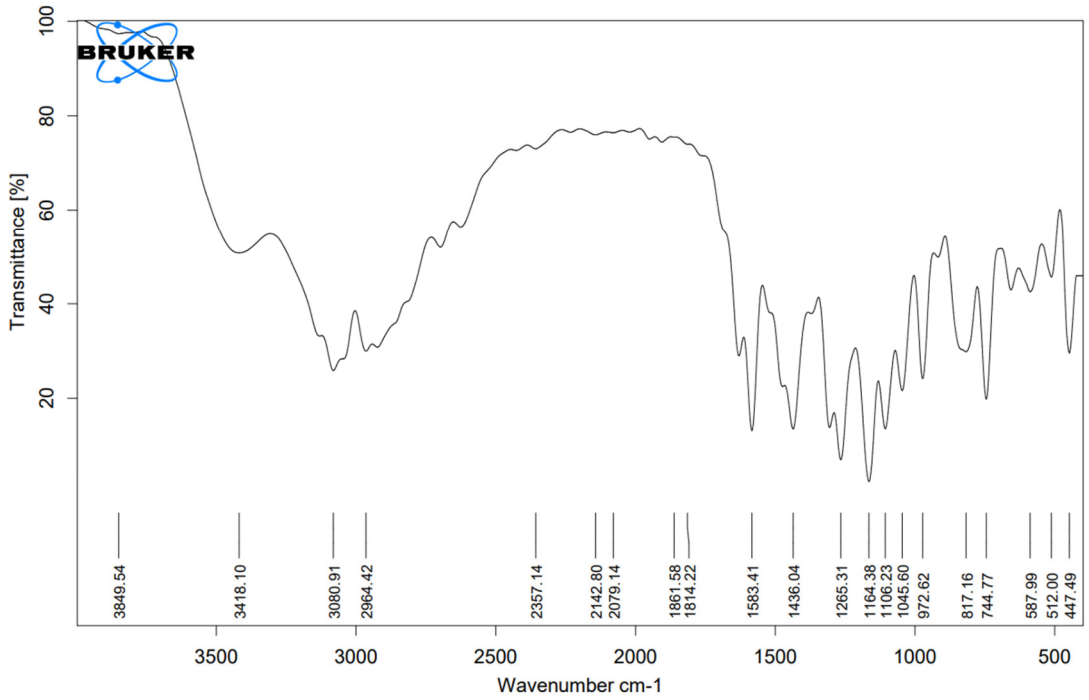

Fig 2: FTIR Spectral analysis of pure DXP

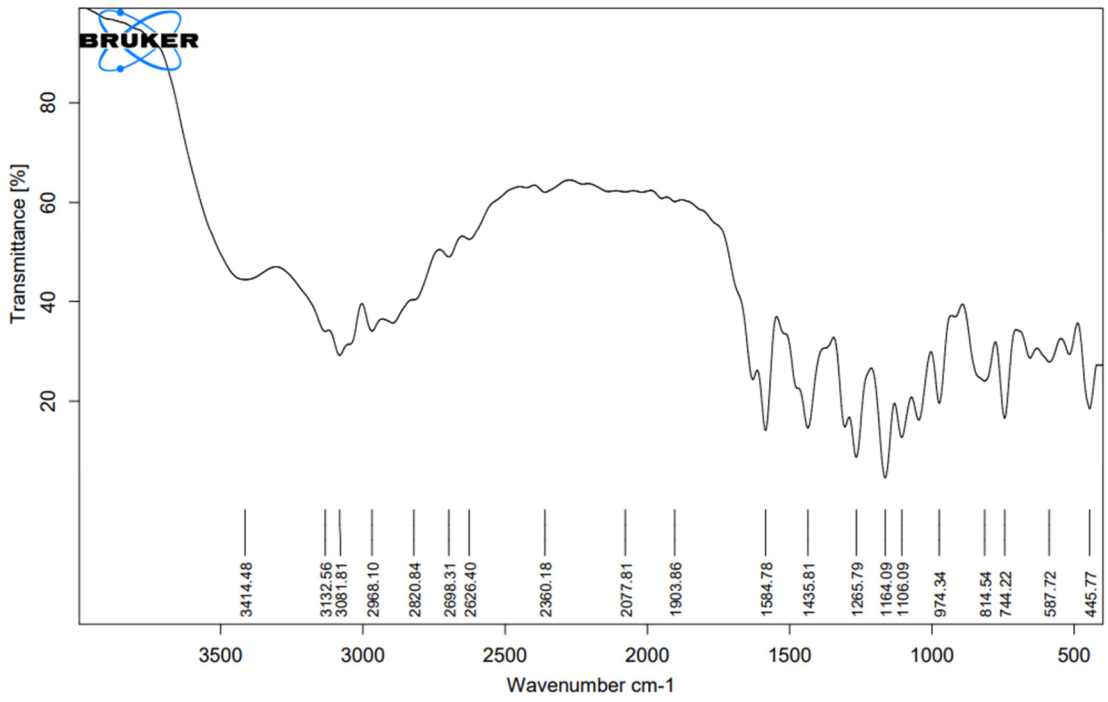

Fig 3: FTIR Spectral analysis of DXP with chitosan

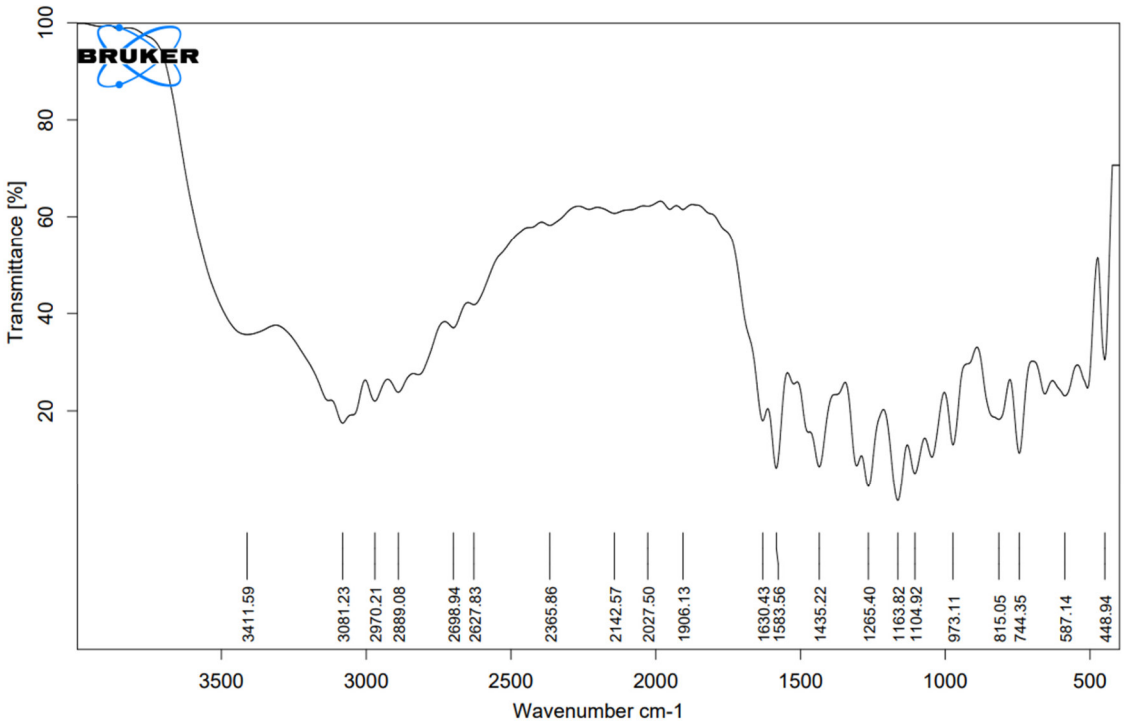

Fig 4: FTIR Spectral analysis of DXP with guar gum

The obtained FTIR spectra are superimposed in the figure 2-4. The observations align with the research literature, and the spectrum distinctly shows the primary identification bands associated with pure DXP. Dexlansoprazole showing N_2H vibration at 3080 cm^{-1}, aromatic ring absorption at 1583 cm^{-1}, ether bond absorption at 1106 cm^{-1}, and sulfonyl absorption at 1045 cm^{-1}. There was no interaction, based on the observed absorption peaks of the drug and excipients.

Evaluation of ODF

The findings are displayed in the Table 2. DF1–DF8 were determined to be 72.16±0.43-284.61±0.47 µm thick. It was discovered that the folding endurance value of DF1–DF12 was 132±6 -183±8. The pH of each film's surface was found to be between 6 and 7 i.e. from 6.03±0.06-6.28±0.11. The disintegration time for DF1–DF8 was 28±4-59±3 sec. According to the data, the disintegration time decreased as the polymer concentration increased.

Table 2: Finding the thickness, folding endurance, and pH of the surface and disintegration time of all formulations

F. Code	Thickness (µm) ± SD	Folding endurance (folds)	Surface pH	In-vitro disintegration Time (sec)
DF 1	102.13±0.62	132±6	6.03±0.06	41±2
DF 2	127.17±0.48	137±5	6.12±0.13	44±4
DF 3	153.57±0.51	145±9	6.14±0.09	52±2
DF 4	178.33±0.64	151±3	6.17±0.11	59±3
DF 5	72.16±0.43	149±6	6.08±0.06	28±4
DF 6	138.28±0.29	162±7	6.16±0.12	30±4
DF 7	216.43±0.58	174±11	6.25±0.14	34±2
DF 8	284.61±0.47	183±8	6.28±0.11	41±4

The weight variation of all formulation varies between 50.28±2.34-179.34±5.21. The results of the drug content % calculations for different formulations ranging in between 94.45±0.17-108.31±0.26. The assay results for each formulation are ranging in between 96.26±2.54-99.39±2.22 displayed in Table 3.

Table 3: Weight variation, drug content uniformity, and assay determination

F. Code	Weight variation	Drug Content Uniformity	Assay
DF 1	115.26 ± 3.16	94.45 ± 0.17	96.26 ± 2.54
DF 2	132.19 ± 7.36	96.28 ± 0.27	98.51 ± 4.35
DF 3	158.21 ± 3.28	95.16 ± 0.18	96.49 ± 3.62
DF 4	179.34 ± 5.21	103.33 ± 0.13	97.62 ± 5.17
DF 5	50.28 ± 2.34	105.53 ± 0.31	96.48 ± 4.02
DF 6	69.32 ± 3.42	108.31 ± 0.26	99.39 ± 2.22
DF 7	88.46 ± 4.36	103.42 ± 0.16	98.71 ± 2.34
DF 8	114.29 ± 3.91	101.28 ± 0.23	96.46 ± 5.12

In-vitro dissolution

For DF1-DF8, the percentage cumulative drug release is shown in Figure 5. Utilizing a Type I USP basket apparatus, the in vitro dissolution investigations were conducted in phosphate buffer with a 6.8 pH. In 20 minutes, DF2 with chitosan 2.5% released 98.04% of the drug; and DF6 with guar gum 1% released 98.65% of the drug. As a result, it is regarded as the ideal formulation.

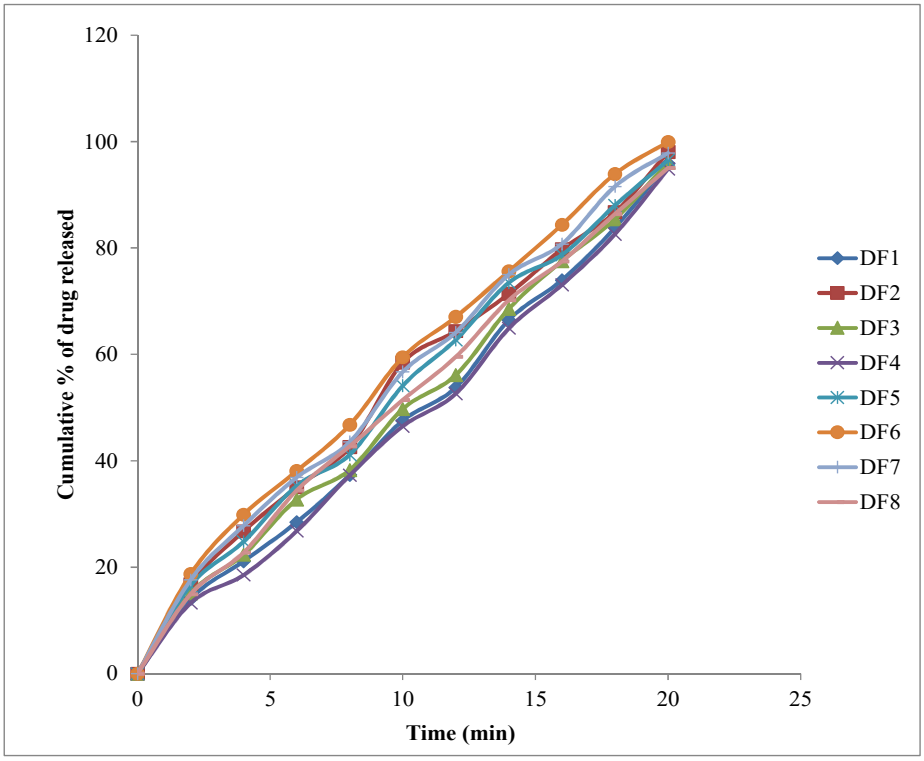

Fig 5: In vitro dissolution studies of formulations (DF1-DF8)

Application of Release Rate Kinetics to Dissolution Data

A variety of models were used to study drug release kinetics. A number of release models, including first-order, zero-order, higuchi, and korsmeyer-peppas, were fitted to the acquired data in order to investigate the medication release rate mechanism of the dose form Kinetics.

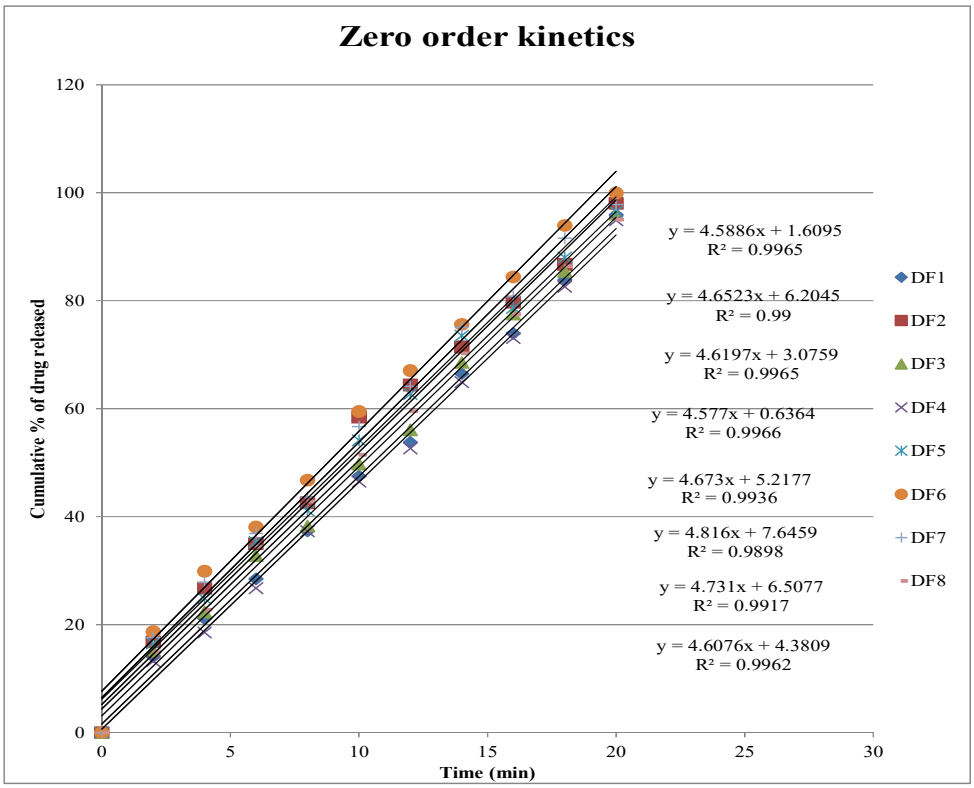

Fig 6: Zero order release kinetics graph of formulations (DF1-DF8)

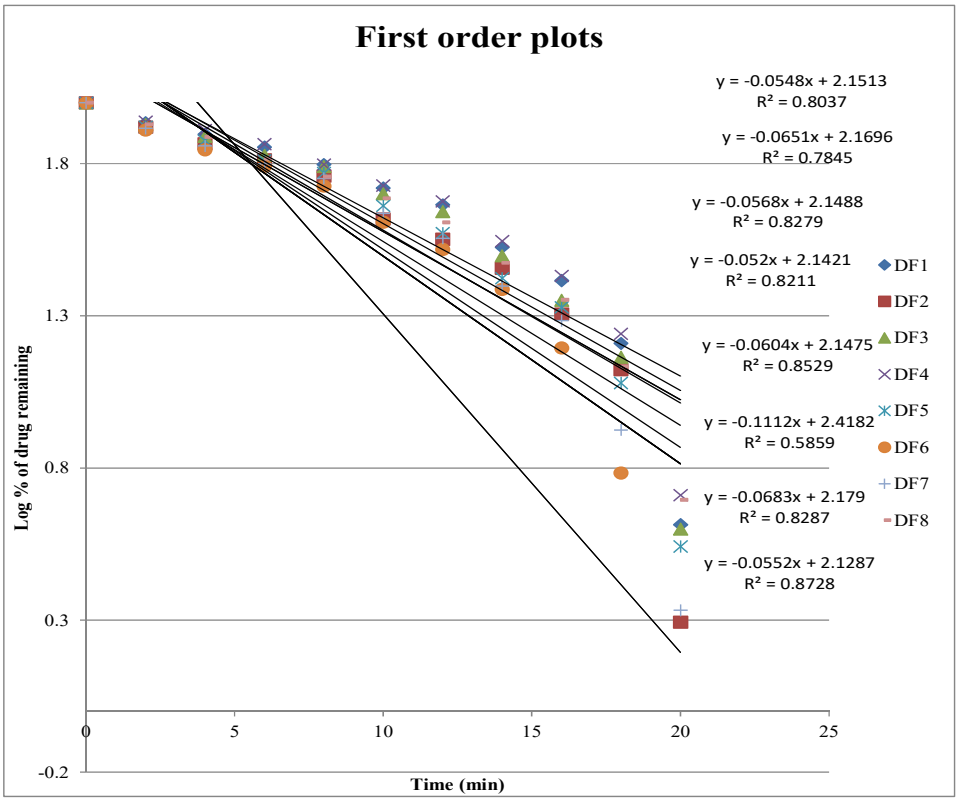

Fig 7: First order release kinetics graph of formulations (DF1-DF8)

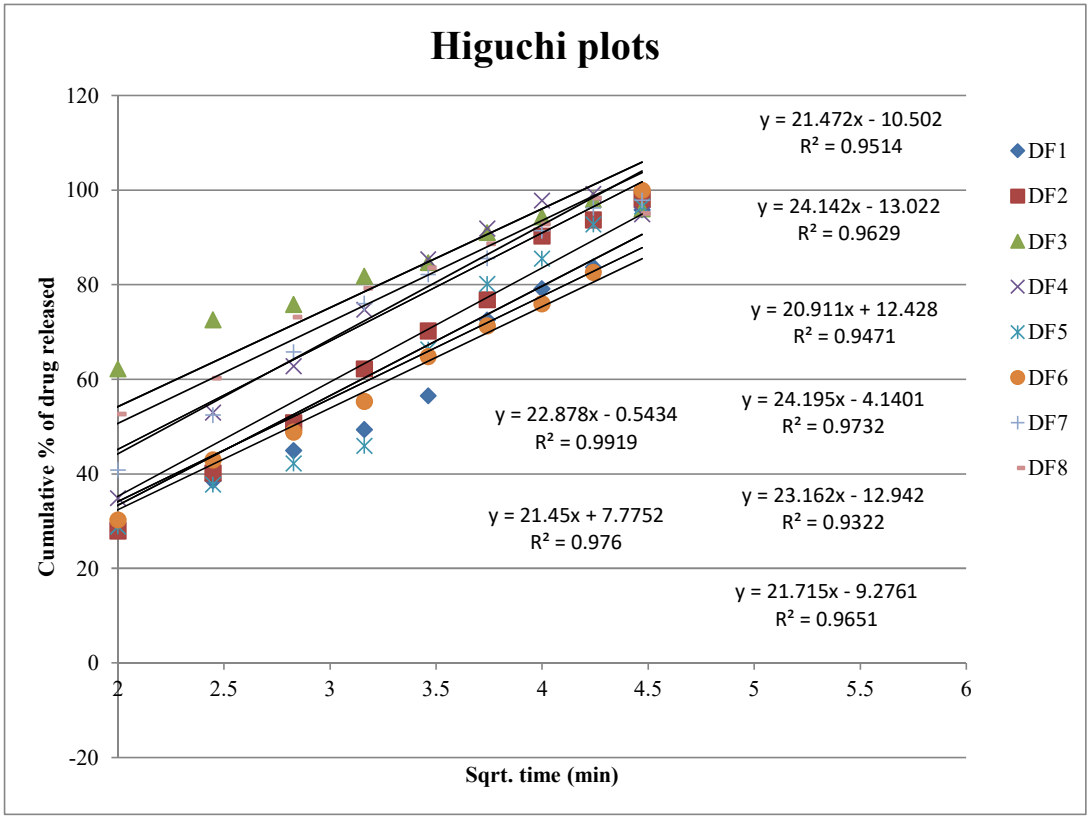

Fig 8: Higuchi release kinetics graph of formulations (DF1-DF8)

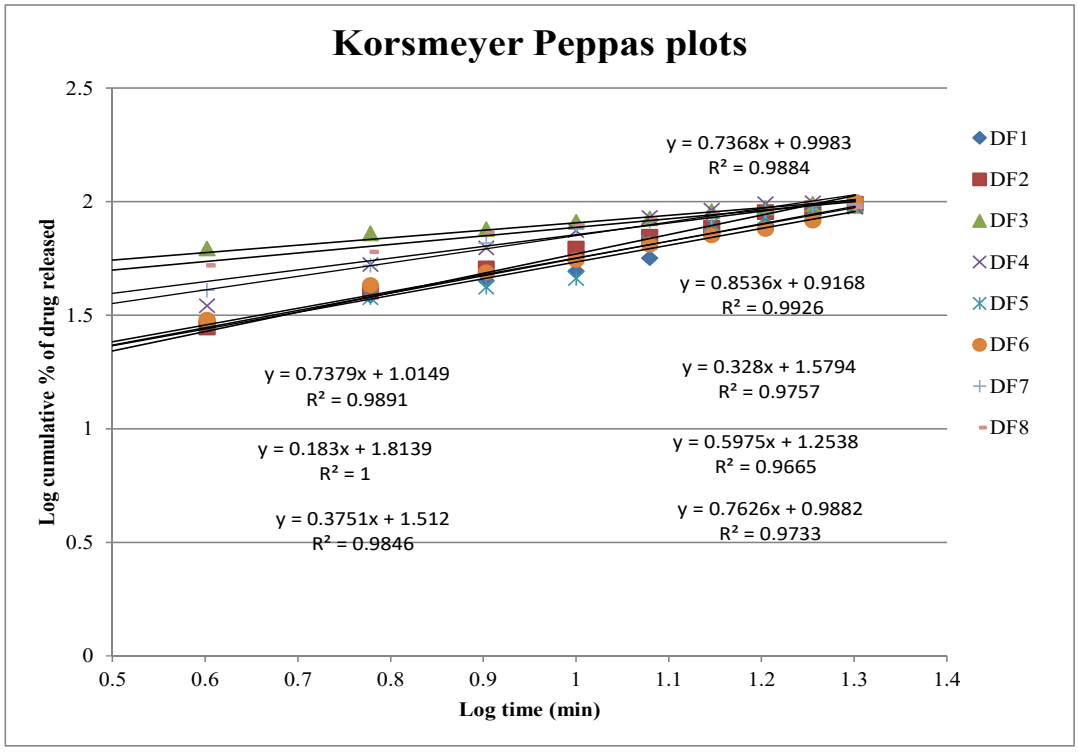

Fig 9: Korsmeyer-Peppas graph of formulations (DF1-DF8)

The drug release kinetics are summarized in Fig. 6 to 9 and indicated that DXP followed zero order release from all the formulations (R^2 0.9898 to 0.9966). It is further noted that all the formulations followed diffusion mechanism of drug release (R^2 >0.6705), and specially formulations DF2 and DF6 which had R2 of 0.9629 and 0.9651 respectively. Koresmeyer peppas equation determines the drug transport mechanism based on the values of coefficient 'n'. If n=0.5 it is Fickian, if n=0.45 to 0.89 then non-Fickian transport, if n=0.89 it is Case II transport, and if >0.89 it is Super case transport. The 'n' values obtained for DF2, and DF6 were 0.8536, and 0.7379 respectively, which indicate that the drug transport mechanism from the DXP was non Fickian.[25] Therefore based on the above data formulations DF2 and DF6 with chitosan 2.5% and guar gum 1% content were optimized.

Stability Studies

According to ICH recommendations, stability studies were carried out to assess the drug formulation's stability. DF2 and DF6 formulations were optimised and packaged in aluminium laminated with polyethylene. Changes in the formulation's colour, drug content, physical appearance, and drug release properties were investigated at the conclusion of the study period. In accordance with ICH requirements, stability experiments were conducted for the optimal formulations at room temperature, 40^0C/75%RH. The drug content percentage was examined at 0, 30, 60, and 90 days, all of which fall within the acceptability range. It follows that the formulation is stable. Table displayed the stability study findings.

CONCLUSION

It was found that the solvent casting method worked well for creating the DXP films that dissolve quickly. Patients with schizophrenia, those who are immobile, or those who are travelling in places without access to water have found success with oral disintegrating films (ODF). Kinetic investigations, stability studies, disintegration time, surface pH, folding endurance, thickness, weight variation, and in-vitro diffusion were among the quality control tests performed on DXP films. The optimised formulations DF2 and DF6 were shown to be stable at accelerated stability conditions. Prepared films showed a faster rate of dissolution and a quicker onset of action, which resulted in better patient compliance, a successful course of treatment, and future growth in popularity.

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