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Formulation and Evaluation of Nicotine Polacrilex Orodispersible Tablet

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Abstract: Nicotine present in tobacco is addictive & makes the process of quitting very prolonged & complex. Nicotine causes pulmonary diseases, lung cancer & heart diseases. Quitting smoking drastically reduces risk of dying from tobacco-related diseases. The current established procedures for smoking cessation have wide variety of side effects. Orodispersible Tablets based on Nicotine Polacrilex were created via direct compression. Preformulation study was performed. Melting point was found to be 80-82˚C by capillary tube method. There was no discernible interaction, indicating compatibility, between the medication and excipients. Pre compression parameters and Post-compression parameters were used to optimize and evaluate the prepared batches and found suitable. Wetting time and water absorption ratio for the best formulation (F3) were determined to be 26.23 seconds and 91.06%, respectively. *In-vitro* drug release for the optimized formulation (F3) was 99.80% within 25 minutes. Based on the aforementioned findings it was concluded that the combination of Cosspovidone and Methyl Cellulose PH 10 was shown to be the best superdisintegration for the preparation of Nicotine Polacrilex Orodispersible.

Keywords: Orodispersible, superdisintegration, Preformulation, Cosspovidone and Methyl Cellulose

INTRODUCTION

Nicotine is a highly addictive drug and many people suffer from its addiction around the globe in the form of smoking[1]. This problem is particularly pronounced in many smokers here do not have access to cessation medications[2]. To prevent smokers from inhaling harmful chemicals like tar, carbon mono oxide and carcinogenic compounds produced from burning vegetable matter, pharmaceutical nicotine is used in the form of orodispersible tablets, chewing gums, TDDS patches and oral films[3]. Oral route is one of most popular routes of drug administration because of its low cost, easy administration and high rate of patient compliance[4]. Many patients mainly geriatric and paediatric ones have dysphagia or have some level of unease when swallowing hard gelatine capsules or solid tablets[5]. This has led to development of orodispersible tablets. Orodispersible tablets are useful in patients such as paediatric, bedridden or developmentally disabled, geriatric patients, many of whom face difficulty in swallowing tablets or hard gelatine capsules[6]. Orodispersible tablets are a novel dosage form in which is prepared using hydrophilic polymers, which rapidly disintegrates or dissolves on the tongue or in the buccal cavity[7].

Orodispersible tablets are most appropriate and convenient dosage form for administration of drug in number of patients like paediatrics (children)geriatrics (old age), psychotic, dysphagic, unconscious patients, for a patients in which there is a condition of undeveloped systems such as muscular and nervous, condition of suffering from hand tremors[8]. The economical method is the main reason behind the popularity of orodispersible tablets for the delivery of active medicament provides a route for active medicament absorption a buccal oral cavity[9]. Orodispersible tablets are also known by synonyms like quick dissolves, orally dissolving tablets[10].

Nicotine present in tobacco is addictive & makes the process of quitting very prolonged & complex[11]. Nicotine causes pulmonary diseases, lung cancer & heart diseases. Quitting smoking drastically reduces risk of dying from tobacco-related diseases[12]. Current established procedures for smoking cessation have wide variety of side effects & in comparison orodispersible tablets are better alternative due to negligible side effects & fast discharge of nicotine.

MATERIALS AND METHODS

Nicotine Polacrilex was obtained from Sai Krishna pharmaceutical Hyderabad as gift, Mannitol was purchased from Mannitol Qindao Bright Moonsea Wood Group Co. Ltd. Sorbitol was International Specialty Product Technologies limited, USA, Methyl Cellulose pH101 from Triveni Chemicals,Vapi Gujrat, India, Crosspovidone from Boai Nky Pharmaceuticals, Thane, India, and other solvents used belongs to L.R. grade.

Method of preparation of Orodispersible Tablets of Nicotine Polacrilex:

A well-known methodology indicates that the direct compression procedure is the simplest and most straightforward way to make tablets. Orodispersible Tablets based on Nicotine Polacrilex were created via direct compression. The drug candidate and other formulation components were weighed with the use of an analytical weighing balance. Aforementioned blend of additives also contained a medication then blended well, after which they were sieved for uniform size. Thereafter, prepared blends were compressed into tablets compressing tablet punching machine by using punch. Punch was 7.00 mm size round flat plain upper punch and plain on lower punch.

Table No. 1: Composition of various batches Oral disintegrating Nicotine Polacrilex tablets

S. No.	Chemicals	F-1	F-2	F-3	F-4	F-5
1.	Nicotine Polacrilex	2 mg	2 mg	2 mg	2 mg	2 mg
2.	Mannitol	35 mg	35 mg	35 mg	35 mg	35 mg
3.	Sorbitol	31.5 mg	31.5 mg	31.5 mg	31.5 mg	31.5 mg
4.	Methyl Cellulose pH101	**32.5 mg**	**31.5 mg**	**30 mg**	**28.5 mg**	**27.5 mg**
5.	Crosspovidone	**2.5 mg**	**3.5 mg**	**5 mg**	**6.5 mg**	**7.5 mg**
6.	Colloidal Anhydrous silica	1.5 mg	1.5 mg	1.5 mg	1.5 mg	1.5 mg
7.	Sucralose	1.5 mg	1.5 mg	1.5 mg	1.5 mg	1.5 mg
8.	Blue spectra flecks	0.2 mg	0.2 mg	0.2 mg	0.2 mg	0.2 mg
9.	Peppermint (Mint flavor)	1.6 mg	1.6 mg	1.6 mg	1.6 mg	1.6 mg
10.	Menthol	0.5 mg	0.5 mg	0.5 mg	0.5 mg	0.5 mg
11.	Magnesium stearate	1.2 mg	1.2 mg	1.2 mg	1.2 mg	1.2 mg

The mannitol and sorbitol were passed through sieve no. (#60) size, separately and sifted into a poly bag then added Nicotine Polacrilex. Above mixture was prepared by proper mixing for 5 min. The crosspovidone super Disintegrating agent, colloidal anhydrous silica as glidant, methyl cellulose PH 101 as tablet bursting and Diluent, sucralose as Sweetner, blue spectra flecks as a coloring agent and peppermint as flavoring agent were mixed together then passed through sieve no. (#60) size. Menthol was sieved through sieve no. (#80) size then mixed it with mixtures prepared in Step-1 and Step-2 in a poly bag for 10 min. The magnesium stearate as lubricant was sifted to mixture prepared in step-3 then mixed well it for 03 (three) min. The prepared mixture was passed through sieve no. (#60). After the screening the required bland was ready for compression. Prepared bland was compressed through tablet punch machine using 7.00 mm punch. Prepared different tablet batches were ready for evaluations.

RESULTS AND DISCUSSION

Preformulation studies

The drug sample was found to be Colorless to light yellow or off white powder with bitter taste and Fish-like odor on warm odor organoleptic characteristic. Found to be 80-82˚C by capillary tube method. Nicotine Polacrilex was insoluble in water, slightly soluble in ethanol, methanol-like organic solvents, soluble in 0.1N HCl weak acids, and soluble in slightly soluble in pH buffers of 6.8.

Scanning and determination of maximum wavelength (lambda λ max): A UV-visible spectrophotometric technique was used to estimate the UV-visible content of Nicotine 6.8 pH calibration curve for phosphate buffer was created and regressed for a straight line. The 0.998 R^2 value indicated good linearity. The calibration curve was following Beer Lambert's law. Nicotine was detected at 260 nm with a maximum concentration against buffer at 6.8 pH as a blank.

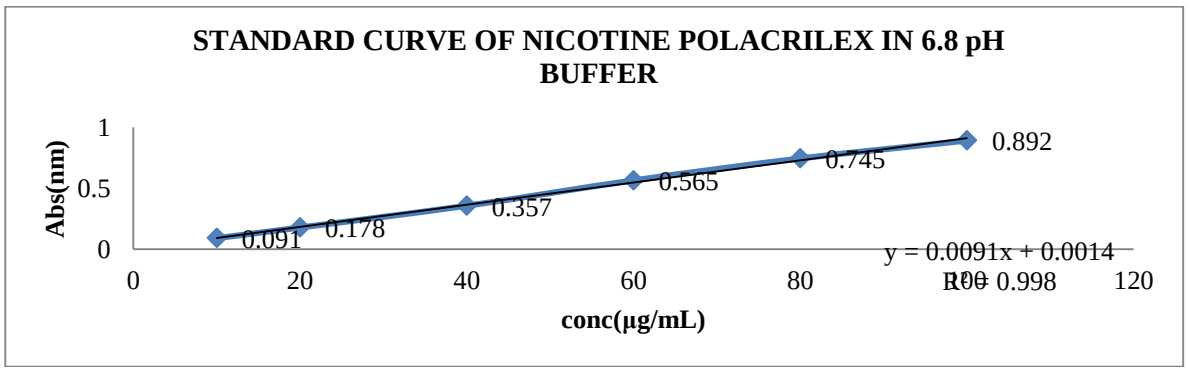

Figure 1: Standard calibration curve for Nicotine in buffer 6.8 pH

Drug polymer compatibility studies by FT-IR spectroscopy: Taken are Nicotine Polacrilex, a natural superdisintegrant and a physical blend of medication and polymer. There was no discernible interaction, indicating compatibility, between the medication and excipients.

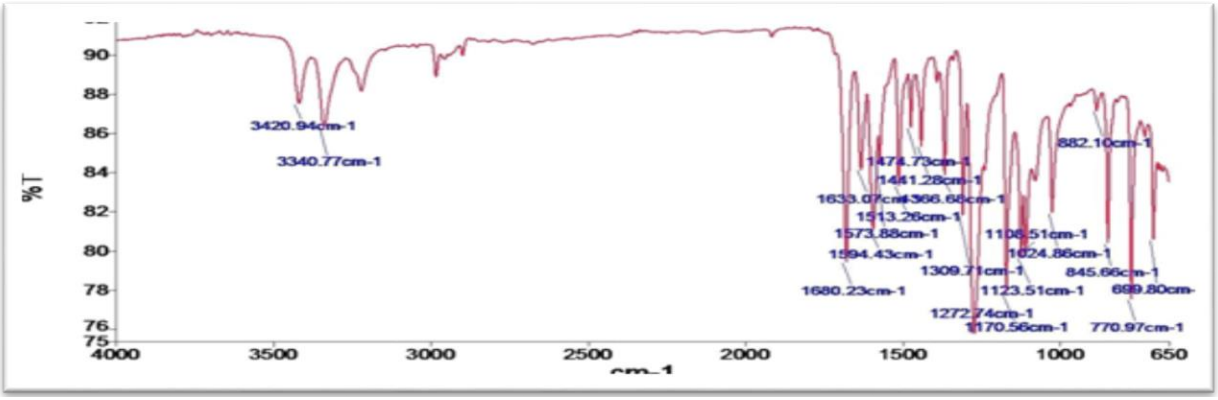

Figure 2: Nicotine Polacrilex FT-IR Spectrum peaks

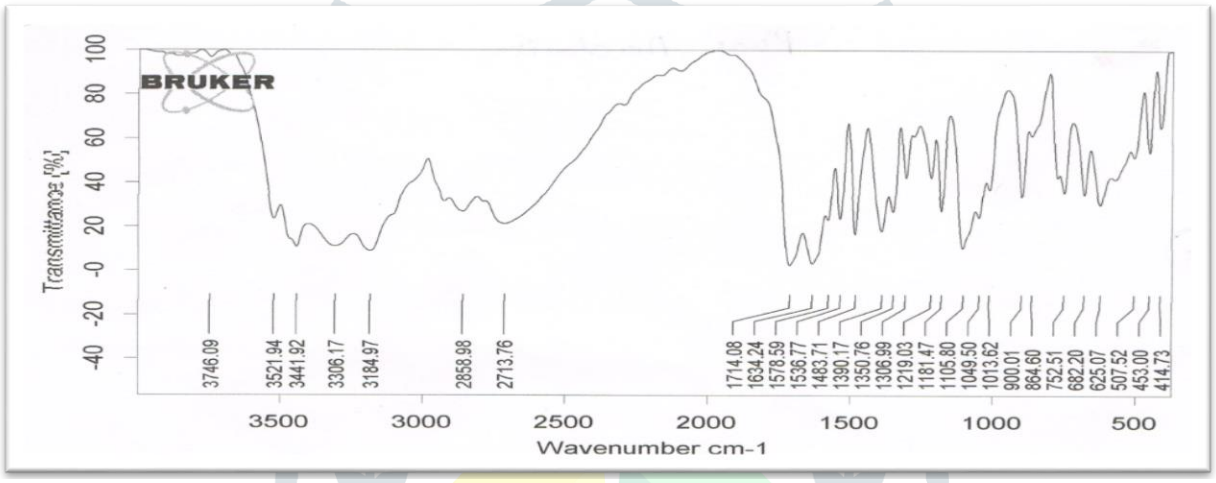

Figure 3: FT-IR Spectrum peaks of optimized formulation (F-3)

Formulation development

Overall, five (F1 to F5) formulations were prepared by direct compression. Each formulation consist of 2 mg of drug Nicotine Polacrilex with Methyl Cellulose pH101 10mg, 20mg, 30mg, 40mg, 50mg and Crosspovidone superdisintegrant of 5mg with other excipients in a measured quantity discussed under section methodology.

Pre-compression Evaluation of Orodispersible Tablets: The angle of repose for the best formulation (F3) was discovered to be 24.28 o. Angles of repose for all formulations ranged from 24.28 o to 30.02 o, demonstrating adequate flow properties. Bulk density for the improved formulation (F3) was determined to be 0.509 gm/cm^3. The bulk density of all formulations was found to range from 0.503 to 0.517 gm/cm3, demonstrating appropriate flow properties. The tapped density of the improved formulation (F3) was discovered to be 0.610 gm/cm^3. The density of all tapped formulations ranged from 0.610 to 0.636 gm/cm^3, which is an acceptable flow characteristic. It was discovered that the optimized formulation's (F3) Carr's index was 11.20%. Carr's index was found to range from 11.20% to 17.38% for all formulations. All formulations exhibit the required compressibility and flow properties. Optimized formulation (F3) Hausner's ratio was found to be 1.125 ± 0.002. All formulations Hausner's ratio were found to be 1.125 ± 0.002 to 1.220 ± 0.002.

Table No. 2: Pre-compression Evaluation of Orodispersible Tablets

Formulation code	Angle of repose (θ)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carr's index (%)	Hausner's ratio
F1	30.02	0.517	0.625	14.88	1.174
F2	29.08	0.503	0.636	15.75	1.187
F3	24.28	0.509	0.610	11.20	1.125
F4	27.40	0.516	0.621	17.38	1.220
F5	26.68	0.504	0.618	16.10	1.191

Post-compression Evaluation of Orodispersible Tablets: The weight variation of the optimized formulation (F3) was discovered to be 200.24mg. For all formulations, the weight variation was determined to be between 199 and 201 mg. It was discovered that the optimal formulation's (F3) hardness was 3.91 kg/cm^2. For all formulations, the hardness was determined to be between 3.91 kg/cm^2 and

4.67 kg/cm^2. All formulations have good mechanical strength as shown by the hardness test. The thickness of the optimized formulation (F3) was discovered to be 3.94 mm. For all formulations, the thickness was determined to be between 3.81 mm and 3.94 mm. Friability for the improved formulation (F3) was discovered to be 0.70%. For all formulations, the friability was observed to range from 0.24 to 0.70%. The drug content of the optimized formulation (F3) was determined to be 99.52%. For all formulations, the drug concentration ranged from 98.42 to 99.52%. Formulations created using the direct compression approach displayed a disintegration time between 20 and 40 seconds. The disintegration time of the optimized formulation (F3) was discovered to be 20 seconds.

Table No. 3: Post-compression Evaluation of Orodispersible Tablets

Formulation code	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	% drug content	*In-vitro* Disintegration time (seconds)
F1	200.78	4.67	3.92	0.24	98.42	40
F2	199.92	4.47	3.90	0.28	98.64	38
F3	200.24	3.91	3.94	0.70	99.52	24
F4	199.79	4.21	3.81	0.53	98.71	12
F5	201.21	4.09	3.88	0.69	99.44	08

Wetting time and water absorption ratio: Wetting time and water absorption ratio for the best formulation (F3) were determined to be 26.23 seconds and 91.06%, respectively. For all formulations, the wetting time and water absorption ratio were determined to be between 26.23 and 40.96 seconds and 84.16 and 91.06%, respectively.

Table No. 4: Wetting time and water absorption ratio of F1-F5

Formulation code	Wetting time(seconds)	Water absorption ratio(%)
F1	40.96	84.16
F2	35.52	86.17
F3	26.23	91.06
F4	31.15	89.09
F5	29.06	89.76

***In-vitro* dissolution studies:** *In-vitro* drug release for the optimized formulation (F3) was 99.80% within 25 minutes. Using an in-vitro dissolving device, a drug research was conducted in vitro for 25 minutes in a phosphate buffer with a pH of 6.8. According to in-vitro dissolution data, formulations F1, F2, and F3 each released 78.881%, 80.598%, and 88.983% of the medication after 20 to 25 minutes, whereas formulations F4, F5, and F6 each released 93.234%, 98.283%, and 99.80% of the drug within the same time frame.

Table No. 5: Comparative percent cumulative drug release of F1-F5 formulations of Nicotine Polacrilex in phosphate buffer 6.8 pH

Time (min.)	F1	F2	F3	F4	F5
0	0	0	0	0	0
0.5	41.95	48.95	49.95	32.75	52.48
1	49.24	53.54	54.24	39.42	53.54
2	53.70	68.71	62.71	40.05	59.54
3	66.01	70.48	74.01	44.29	65.54
4	74.36	80.36	80.36	48.14	70.12
5	71.25	83.54	92.37	66.03	80.36

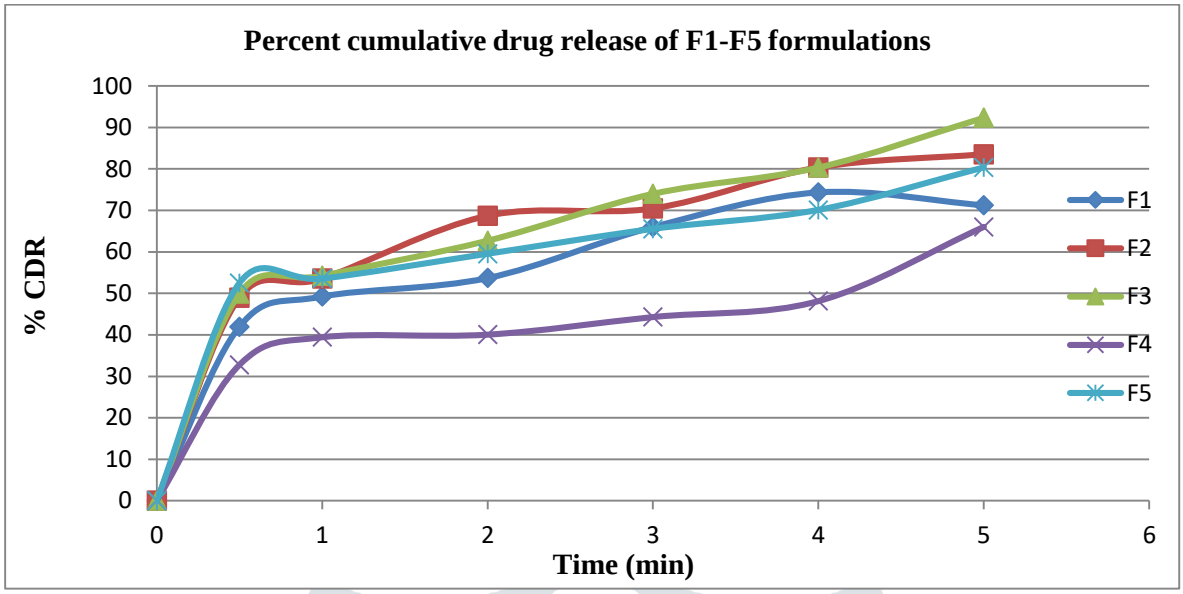

Figure 4: All formulation F1-F5 in- vitro dissolution profile in phosphate buffer pH 6.8

CONCLUSION

The Orodispersible Tablets formulation provides speedy release of the medicine and is based on Nicotine Polacrilex. The direct absorption of these tablets into the systemic circulation was occurred. When FT-IR indicated that a medicine and its excipients were compatible, it meant that there was no physico-chemical interaction between the two. Cosspovidone and Methyl Cellulose PH 101 were used as superdisintegrant effectively create drug-based orodispersible Tablets utilizing the direct compression method and these tablets were determined to be better since they did not chip, cap, or stick. Drug distribution inside the formed tablet is uniform, as seen by the identical drug content in every prepared tablet. Out of all five tablet batches that were created, tablet formulation number F3 offers the medication 92.37 % of its maximal release. It was discovered that the optimized formulation F3 worked well with all parameters. The formulation F3 was determined to be the best among all developed formulations based on the findings of disintegration time and dissolving profile. Based on the aforementioned findings that the combination of Cosspovidone and Methyl Cellulose was shown to be the best superdisintegration for the preparation of Nicotine Polacrilex Orodispersible.

CONFLICTS OF INTERESTS

There are no conflicts of interests.

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