International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 8, Issue 8, 2016

Original Article

DESIGN AND DEVELOPMENT OF *NICOTIANA TABACUM* FILM USING FACTORIAL DESIGN

ANWAR DAUD[1], ASHOK PEEPLIWAL[1], MINAL BONDE[2], NIDHI SAPKAL[3] NARESH GAIKWAD[4]

[1]Department of Pharmaceutical Science, NIMS University, Jaipur, [2]Zim Laboratories Ltd., Nagpur-441501, [3]Gurunanak College of Pharmacy, Nagpur, [4]Department of Pharmaceutical Science, RTM Nagpur University, Nagpur, India

Received: 25 Mar 2016 Revised and Accepted: 20 May 2016

ABSTRACT

Objective: The objective of the present investigation was to develop and optimize *Nicotiana tabacum* oral dissolving films with optimized physicomechanical and chemical properties for improved patient compliance. *Nicotiana tabacum* oral dissolving films are used to help people stop smoking cigarettes.

Methods: *Nicotiana tabacum* oral dissolving films were prepared by solvent casting method using hydroxymethylpropyl cellulose as film forming polymer and polyethylene glycol 6000 as a surfactant. The process was optimized using the design of experiments. Four process parameters were studied at two levels using 2^4 design. Further, the optimized *Nicotiana tabacum* oral dissolving films were evaluated for HPTLC analysis, microbial limit test, organoleptic evaluation, stability studies and clinical efficacy studies.

Results: It was found that the thickness of wet film and viscosity of solution has a significant influence on thickness as well as disintegration time. Folding endurance and tensile strength of the film was influenced by the thickness of the wet film, machine speed and viscosity of the solution. Drying temperature does not have any significant influence on the selected response. By controlling the thickness of wet film 0.5 mm, the viscosity of the solution 5000 cps and machine speed 15 min, disintegration time, folding endurance and tensile strength of this formulation can be controlled.

Conclusion: It was noted that *Nicotiana tabacum* oral dissolving films are being accepted by patients in general and showed a marked reduction in craving for smoking. Prepared formulation was stable for 6 mo stability as per ICH guidelines.

Keywords: *Nicotianna tabacum*, Factorial designs, Pilot scale clinical efficacy studies

INTRODUCTION

Cigarette causes the early death of nearly 5 million people each year. These people are not killed by the nicotine in the cigarette, but by other constituents of tobacco smoke such as carbon monoxide and the other 4000 chemicals present in tobacco. Out of the major cigarette smoke constituents only nicotine has stimulant and depressant property while all others have been categorized as carcinogenic, cytotoxic, tumor accelerator and poisonous [1]. Nicotine replacement therapy (NRT) helps to damp down the urges to smoke that most smokers have in the early days and weeks after quitting. It gives the smoker the chance to break smoking cues in their daily lives, and might provide a more comfortable exit from the smoking habit. NRT is a way of getting nicotine into the bloodstream without smoking. There are nicotine gums, patches, inhalers, tablets, lozenges and sprays [2]. No oral dissolving films (ODFs) have been reported. Thus the aim of the present investigation is to develop and optimize ODFs of *Nicotiana tabacum* (NT) Linn with ideal physicomechanical and chemical properties with improved patient compliance and convenience.

ODFs are gaining popularity among drug delivery systems for delivering medicament to pediatric, geriatric and many other patients due to a high degree of patient convenience. This dosage form exhibits better patient compliance during travelling as there is no need of water to swallow the dosage form. These are thin films and when kept on the tongue these dissolve rapidly and deliver unit dose accurately.

MATERIALS AND METHODS

Materials

Nicotiana tabacum extract was procured as a gift sample from Unijules Life Science Limited, Nagpur, India. HPMC 15 cps, tween 80, mentha oil and spearmint oil were procured from SD Fine Chemical Lab., A. B. Enterprises, and Mumbai, India. All other chemicals and reagents were of analytical grades. Deionized double-distilled water was used throughout the study.

Preparation of *Nicotiana tabacum* ODFs

ODFs of NT extract were prepared using solvent casting method [3]. The composition of the formulation is presented in table 1. NT 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 NT, successively measured amount of HPMC, PEG6000, polysorbate 80, sweetening and flavoring agents were added and the solution was stirred for 30 min. The thick, viscous solution was degassed to remove entrapped air by ultrasonication. The solution was then cast on a glass plate to uniform thickness and dried in hot air oven. The films were stored in aluminium foil and air tight polythene packs in desiccators until further use.

Table 1: Composition of prototype formulation of *Nicotiana tabacum ODFs*

Ingredients	mg/film
Nicotiana tabacum	20
HPMC 15 cps	55
PEG 6000	15
Polysorbate 80	10
Sucralose	1
Menthe oil	1
Distilled water	Q. S.

Study of the effects of process parameters A factorial design evaluating 4 factors at two levels was studied

using full-factorial design consisting of 24 = 16 runs. Four independent factors, namely thickness of wet film (A), drying temperature (B), machine speed (C) and viscosity of the solution (D) were identified as critical process parameters. Table 2 shows lower and upper limits of these critical process parameters. Effect of critical process parameters was studied on the thickness of the dry film (Y1), in vitro disintegration time (Y2), folding endurance (Y3) and tensile strength (Y4), which were selected as response parameters.

The factorial design was carried out using the software Design Expert version 8.0.6 (Stat-Ease Inc., Mineapolis, USA). Response surface graphs were used to determine the factor of interaction between the considered variables. Values of "Prob>F" less than 0.0500 indicates model terms are significant. Values greater than 0.1000 indicate the model terms are not significant. A factor was considered to influence the response if the effects are significant ($p<0.05$). A positive value indicates a synergistic effect that favors optimization, while a negative sign represents an antagonistic effect or the inverse effect of the factor on the selected response [4].

The formulations were formulated as per the full factorial design. The formulation codes of all 16 batches of NT ODFs are listed in table 3.

Table 2: Variables and their levels were chosen for the optimization of ODFs

Variables levels	Low (-1)	High (+1)
Thickness of wet film	0.50 mm	0.75 mm
Drying temperature	80 °C	120 °C
Machine speed	0.1 min	0.3 min
Viscosity of the casting solution	15 cps	20 cps

Table 3: Full factorial design (2^4) layout on process parameters for NT ODFs

	Variable in coded value			
Batch	**A**	**B**	**C**	**D**
NT1	0.5	80	0.1	15
NT2	0.75	80	0.1	15
NT3	0.5	120	0.1	15
NT4	0.75	120	0.1	15
NT5	0.5	80	0.3	15
NT6	0.75	80	0.3	15
NT7	0.5	120	0.3	15
NT8	0.75	120	0.3	15
NT9	0.5	80	0.1	20
NT10	0.75	80	0.1	20
NT11	0.5	120	0.1	20
NT12	0.75	120	0.1	20
NT13	0.5	80	0.3	20
NT14	0.75	80	0.3	20
NT15	0.5	120	0.3	20
NT16	0.75	120	0.3	20

Thickness of wet film (A), Drying temperature (B), Machine speed (C), Viscosity of the casting solution (D)

Characterization of Nt ODFs

The NT ODFs were characterized for following physico-chemical and mechanical parameters.

Appearance of films

ODFs of all the batches were evaluated for their appearances and were categorized as transparent or translucent and smooth or rough surface [5].

Tack test/Dryness test

Tackiness of ODFs was determined in which a film was allowed to adhere to a piece of paper, which was then pressed. Total ten films were stacked for seven days at ambient conditions in a cassette and on the seventh day were observed for sticking properties. Good quality films should not stick to the piece of paper as well as to each other [6, 7].

Thickness

The thickness of a film was measured using calibrated electronic digital micrometer (IP 65, Mitutoyo Co., Japan). Ten films from each batch were taken randomly and their thickness was measured and the mean value was calculated [8].

Folding endurance

Folding endurance was determined by repeated folding of the film at the same place till the film breaks. The number of times the film is folded without breaking was computed as the folding endurance value [9].

Tensile strength

The tensile strength of the film was determined by tensile strength instrument (Suarashtra systopack Pvt. Ltd., Mumbai). To determine tensile strength, a film was placed between corked lined iron plates. One end of the film was kept fixed with the help of an iron screw and the other end was connected to a freely movable iron screw over a pulley. Tensile strength is the maximum stress applied to a point at which the film specimen breaks [10, 11]. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip.

Disintegration test

Disintegration test was performed in the USP disintegration apparatus (Electrolab, Mumbai). Simulated salivary fluid was placed in the tubes of the container and the discs were placed over it. Time after which ODFs lose its integrity was noted as disintegration time. The average *in vitro* disintegration time of six films from each formulation was noted and the mean was reported [12].

Surface morphology determination

For this study, a small section of each ODF was cut and then mounted onto stubs using double sided adhesive tape. Then the sections were examined under scanning electron microscope (Phenom desktop SEM) for surface morphology [13].

Content of NT ODFs by HPTLC [14]

ODFs containing extract equivalent to 100 mg of raw herb from each formulation were picked randomly, weighed individually and analyzed for the quantitative estimation as per the following methods.

Preparation of test solution

Films containing NT extract equivalent to 5 g of raw herb from each formulation were picked randomly and weighed individually. Films were agitated in methanol for 45 min and then it was cooled, filtered. The remaining residues were refluxed again with 30 ml ethanol for 20 min. Then it was cooled, filtered and washings were combined. This was then concentrated on a water bath and reconstituted with 10 ml of methanol.

Reference solution: The reference standard was prepared with 10 mg reference standard of nicotinic acid.

Chromatographic condition

Stationary phase-HPTLC precoated, silica gel 60, F 254 (Merck)

Thickness-0.2 mm

Mobile phase-Toluene: Ethyl Acetate: Diethylamine (7:2:1)

Scanning wavelength-230 nm

Visualization aid-through UV-cabinet under 254 nm and 366 nm and under daylight also.

Spray reagent-Anisaldehyde sulphuric acid reagent

Stability studies

The optimized batch was kept for stability studies as per ICH guidelines Q (R1) for the period of 6 mo. Conditions selected are as follows:

- 40 °C±2 °C/75%±5% RH
- 30 °C±2 °C/75%±5% RH

During storage, the ODFs were evaluated for their physical appearance, tackiness, *in vitro* disintegration time and quantitative estimation of Nicotine [15-17].

Microbiological limit test

This test was designed to determine total aerobic microbial, yeast and mould count. This test also demonstrated that the product is free of *Staphylococcus aureus, Escherichia coli and Pseudomonas aeruginosa, Salmonella, C. albicans and A. niger*. The microbiological limit test was performed according to the specification given in Indian Pharmacopoeia [18].

Organoleptic evaluation

The final formulation qualifying the stability test was subjected to organoleptic evaluation. The objective of these studies was to check the acceptability of NT ODFs in human volunteers who were on the treatment of nicotine withdrawal therapy. Ten volunteers were selected and they were informed about the purpose of the study and study protocol. A written consent form was supplied, understood and signed by each subject prior to dispensing of test materials. All subjects were allowed to place one strip on the tongue and asked to evaluate on the basis of three parameters: physical appearance, taste and after taste [19]. The key for evaluation are given in table 4.

Table 4: Evaluation of organoleptic characteristics of ODFs

Parameters	Physical appearance	Taste	After taste
0	Not good	Not good	Not bitter
1	Acceptable	Palatable	Slightly bitter
2	Good	Good	Bitter
3	Excellent	Excellent	Very bitter

Pilot scale clinical efficacy test

Ethics committee approval was taken from COMSARTs (Committee for Safety and Rights of Trial Subjects on 06.01.2011). These trials were conducted at the clinic of an Ayurvedic physician for the period of two weeks for each trial. All the subjects were completely informed concerning the pertinent details and the purpose of the study. In the present study, most of the patients belong to the age group of 25 to 40 y.

A written consent form was supplied, understood and signed by each subject prior to dispensing the ODFs of NT. All the clinical studies were conducted on the 10 volunteers from each clinical condition. The effectiveness of ODFs, for all the conditions was rated as below:

100 %	Complete reduction in craving
75 to 100 %	Significant reduction in craving
50 to 75 %	Moderate reduction in craving
25 to 50 %	Mild reduction in craving
Up to 25 %	No reduction in craving

RESULTS AND DISCUSSION

The developed ODFs of NT shows easy separation from the surface and found translucent and non tacky as reported in table 5. Effect of critical process parameters with their F-values and p-values is given table 6.

From the results of table 6, it was noted that the thickness of the dry film is significantly influenced by the thickness of the wet film (A) and viscosity of dispersion (D) with probability values of 0.0001 for both of these factors. Response surface graphs were plotted for these two for the thickness of the dry film. As shown in fig. 1**, the** viscosity of dispersion and thickness of wet film showed a synergistic effect on the thickness of the dry film. As the viscosity of dispersion and thickness of wet film increased, there was an increase in thickness of the dry film. Both drying temperature (B) and machine speed (C) were not showing any significant effect on the thickness of the dry film.

For second response Y2 (disintegration time), all the critical process parameters, i.e. thickness of wet film (A), drying temperature (B), machine speed (C) and viscosity of dispersion (D) with a p values of 0.0001, 0.0026, 0.0007 and 0.0001 respectively were found to be significant factors. The interaction between factor A and C was also seen with a p value of 0.0424. From fig. 2, it was noted that with an increase in wet film thickness there was an increase in disintegration time. This is obvious as increased wet film thickness, results in thicker dry films and thicker films have longer disintegration time. Similar results were reported by the Bruce C. in his patent application of Melt extruded thin strips containing coated pharmaceutical actives [20]. This is because disintegration medium has to penetrate more internal surfaces so that disintegration can be made. The viscosity of dispersion, the thickness of wet film and drying temperature showed positive effects on disintegration time, as increased in the level of these factors, resulted in increased disintegration time as shown in fig. 3 to 5.

Factors A, C and D showed the influence on Y3 (folding endurance) having p values of 0.0064, 0.0145 and 0.0003 respectively. Factor A and C showed an antagonist effect while factor D showed synergistic effect, table 6. This is obvious as an increase in thickness of the wet film will result in thicker dry films that will have lower folding endurance as thicker films are less flexible. Similarly, faster machine speed will result in films with higher folding endurance. From the response surface plots for folding endurance fig. 6 and 7, it was observed that factors A, C and D showed a significant effect on the folding endurance of the NT ODFs.

As shown in table 6, on response Y4, factors A, B, C and D showed significant influence. For response Y4, factor A showed a synergistic effect with F values of+48.000 while factor B, C and D had the antagonistic effect of-0.425,-35.000 and-1.200 respectively. From fig. 8, for response Y4, it was observed that factor A and B showed antagonistic effect. If the level of factor A is increased from low level to high level, it results in an increase in tensile strength of NT ODFs. While factor B when increased to a high level, it reduces the tensile strength of films of NT ODFs. Higher drying temperature will result in dryer films. Previous researchers have reported the role of moisture as a plasticizer in films [21]. A lesser quantity of moisture means lesser flexibility in films.

Thus, from the above studies, it was noted that, when NT ODFs was casted at thickness (A) 0.5 mm, drying temperature (B) 80 °C, machine speed (C) 0.3 m/min and viscosity of dispersion (D) 15 cps, the ODFs obtained had shown good physical appearance, having thickness 0.046 mm, disintegration time 5 s, folding endurance 37, tensile strength 28 N/mm^2, percentage elongation 53%. Therefore formulation NT5 was further selected for HPTLC analysis, microbial limit test, organoleptic evaluation, stability studies and clinical efficacy studies.

Fig. 9 shows scanning micrographs of NT ODF. From the fig., it was observed that the surface morphology showed smooth surfaces indicating uniform distribution of formulation ingredients. All ingredients were also miscible which shows that nature of chemical constituents of NT extract is hydrophilic that results in complete mixing between them. Fig. 10 gives densitogram of ginger extract. Fig. 11 gives a calibration curve of principle peak at different concentrations. R^2 value was found to be 0.995. This calibration curve was used for calculating percent extract content in the formulated ODFs.

The microbial limit test was performed on the optimized formulation of NT5 ODFs and results are given in table 7. The study was carried out for a period of three months. From the results obtained it was concluded that formulation NT ODFs was free from microbial contamination as the cfu/g values for the total microbial count were in the limit of NMT 1000 cfu/g i.e. 180 cfu/g in 1 mo, 198 cfu/g in 2 mo and 216 cfu/g in 3 mo. The total yeast count was also in the limit of 100 cfu/g and all other specified micro-organism such as *Escheria coli, Salmonella, Pseudomonas aeruginosa, Staphylococcus aureus* were also absent. Thus, it can be concluded that water and other excipients present are not posing any threat to the microbial stability of these formulations.

The results of the organoleptic characterization of NT5 ODFs are shown in table 8 [key in table 4]. From the results obtained for NT5 ODFs, although scored 23 points out of 30 for taste but none of the volunteers reported any bitter aftertaste. This demonstrates that these ODFs will also be acceptable by patients in general.

The results of stability studies of NT ODFs are given in table 9. When NT ODFs formulations were stored at 40 °C±2 °C and 75%±5% RH, 30 °C±2 °C and 75%±5% RH there was no apparent changes observed in physical appearance (i.e. shape, color, flexibility) and tackiness. The formulation was stable when subjected to the disintegration test and quantification test and was found to be almost constant for up to 6 mo regardless of storage conditions. There was no significant change in the selected criteria as per ICH guidelines.

The studies for the evaluation of clinical efficacy of NT5 ODFs were conducted on the 10 human volunteers who were on the treatment of nicotine withdrawal therapy. From table 10 it was noted that reduction in craving for smoking was 85.98%. This study supports the use of NT ODFs in nicotine withdrawal therapy in conjunction with a behavioral support program NT ODFs are specially recommended for this therapy as this does not have the risks associated health as in the case with cigarettes smoking. Because these films are free of tar, carbon monoxide and other toxins that are found in cigarette smoke. These films will simply satisfy the craving for smoking.

Table 5: Results of 2^4 factorial design on physicomechanical properties of NT ODFs

Formulation code	Separation from the surface	Appearance of film	Tack test	Thickness (mm)	Disintegration test (s)	Folding endurance	Tensile strength (N/mm^2)
NT1	Separate	Translucent	Not tacky	0.045±0.12	8±0.19	31±0.13	24±0.29
NT2	-do-	-do-	-do-	0.059±0.18	19±0.18	42±0.14	34±0.18
NT3	-do-	-do-	-do-	0.045±0.19	13±0.18	28±0.17	22±0.72
NT4	-do-	-do-	-do-	0.062±0.18	23±0.21	36±0.26	29±0.82
NT5	-do-	-do-	-do-	0.046±0.11	5±0.19	37±0.19	28±0.28
NT6	-do-	-do-	-do-	0.061±0.19	9±0.17	48±0.19	38±0.28
NT7	-do-	-do-	-do-	0.047±0.21	8±0.18	37±0.23	22±0.86
NT8	-do-	-do-	-do-	0.061±0.18	18±0.18	42±0.61	31±0.71
NT9	-do-	-do-	-do-	0.065±0.24	20±0.21	55±0.18	29±0.29
NT10	-do-	-do-	-do-	0.078±0.28	32±0.28	59±0.34	38±0.71
NT11	-do-	-do-	-do-	0.066±0.19	24±0.28	40±0.45	27±0.34
NT12	-do-	-do-	-do-	0.073±0.27	33±0.17	68±0.41	34±0.57
NT13	-do-	-do-	-do-	0.062±0.19	16±0.18	65±0.42	31±0.74
NT14	-do-	-do-	-do-	0.079±0.25	22±0.27	80±0.35	39±0.13
NT15	-do-	-do-	-do-	0.065±0.15	21±0.23	57±0.39	32±0.87
NT16	-do-	-do-	-do-	0.077±0.01	26±0.29	73±0.25	42±0.76

Note: All the values are expressed as mean±standard deviation; n=3

Table 6: The quantitative factor effects (F values) and associated p-value for all four responses for NT ODFs

Source	Y1 (Thickness)		Y2 (Disintegration test)		Y3 (Folding endurance)		Y4 (Tensile strength)	
	F Value	p-value	F Value	p-value	F Value	p-value	F Value	p-value
A	+0.10850	0.0001	+58.50000	0.0001	-85.00000	0.0064	+48.00000	0.0003
B	+2.78125E-004	0.9123	+0.20312	0.0026	-0.19375	0.1598	-0.42500	0.0387
C	-0.015000	0.5878	+6.25000	0.0007	-32.50000	0.0145	-35.00000	0.0217
D	+5.87500E-003	0.0001	+3.57500	0.0001	+0.85000	0.0003	-1.20000	0.0026
AB	-2.25000E-004	0.3451	+0.025000	0.8797	+0.40000	0.4963	-0.100000	0.6341
AC	+0.035000	0.4545	-85.00000	0.0424	-20.00000	0.8617	+20.00000	0.6341
AD	-2.20000E-003	0.2588	-0.60000	0.6529	+5.60000	0.2556	-0.40000	0.8102
BC	+9.37500E-005	0.7425	+0.21875	0.3155	-0.18750	0.7943	+0.12500	0.6341
BD	-8.75000E-006	0.4545	-8.75000E-003	0.3155	-7.50000E-003	0.7943	+0.022500	0.0717
CD	-7.50000E-004	0.7425	-0.25000	0.8797	+6.50000	0.2869	+1.50000	0.4818

Note: A-Thickness of wet film, B-Drying temperature, C-Machine speed, D-Viscosity of dispersion

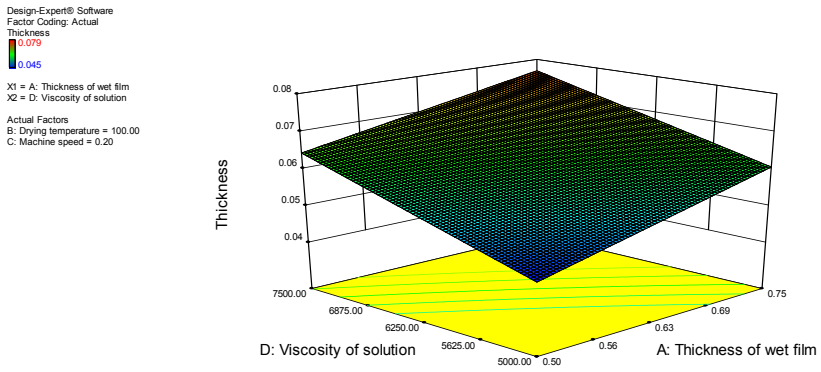

Fig. 1: Surface response plot showing the viscosity of dispersion and thickness of wet film on thickness of NT ODFs

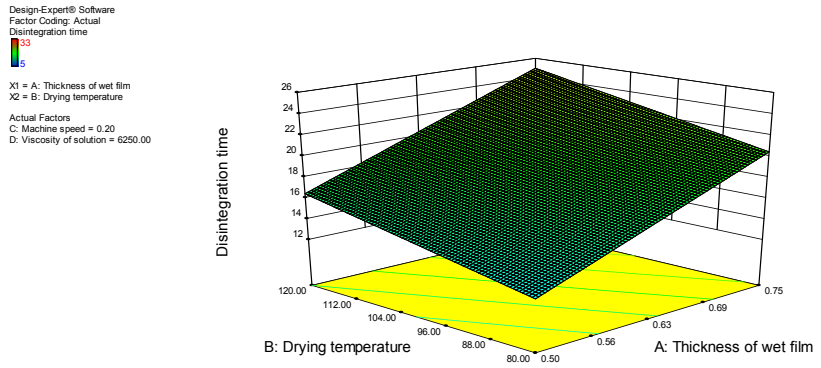

Fig. 2: Surface response plot showing the drying temperature and thickness of wet film on disintegration time of NT ODFs

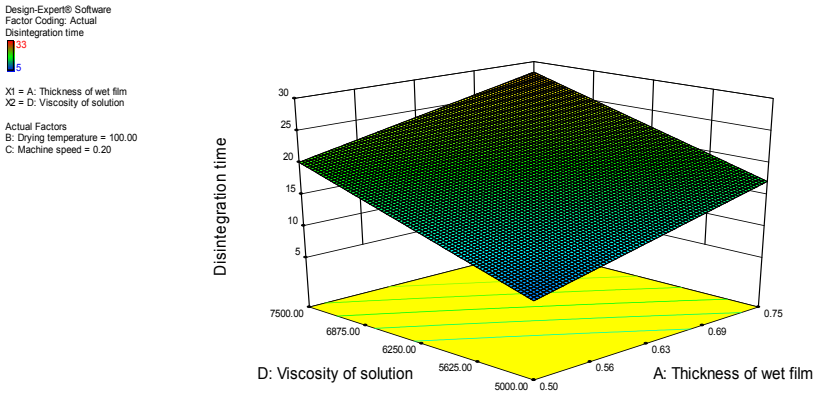

Fig. 3: Surface response plot showing the viscosity of dispersion and thickness of wet film on disintegration time of NT ODFs

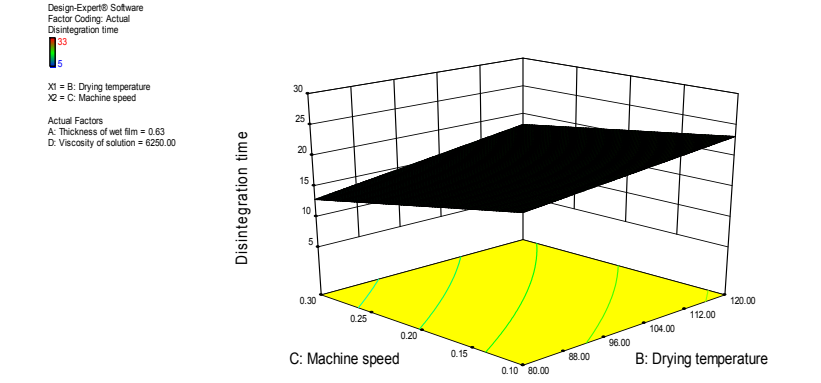

Fig. 4: Surface response plot showing the machine speed and drying temperature on disintegration time of NT ODFs

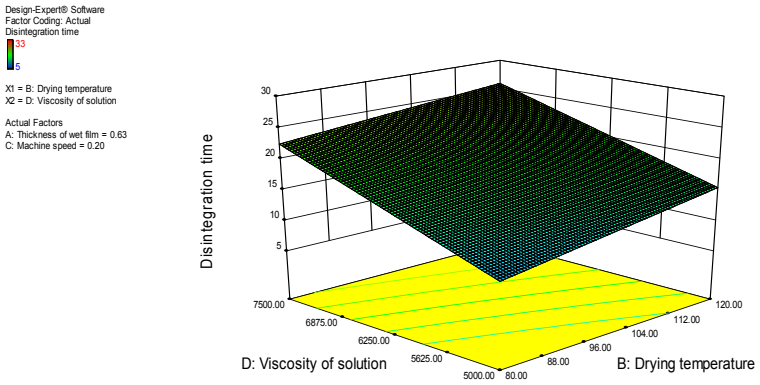

Fig. 5: Surface response plot showing the viscosity of dispersion and drying temperature on disintegration time of NT ODFs

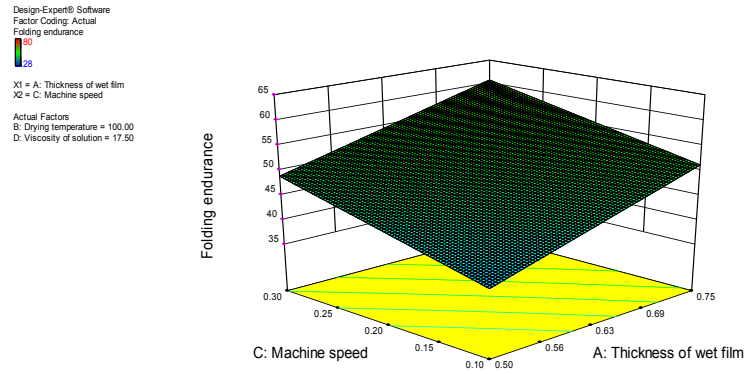

Fig. 6: Surface response plot showing the drying temperature and thickness of wet film on folding endurance of NT ODFs

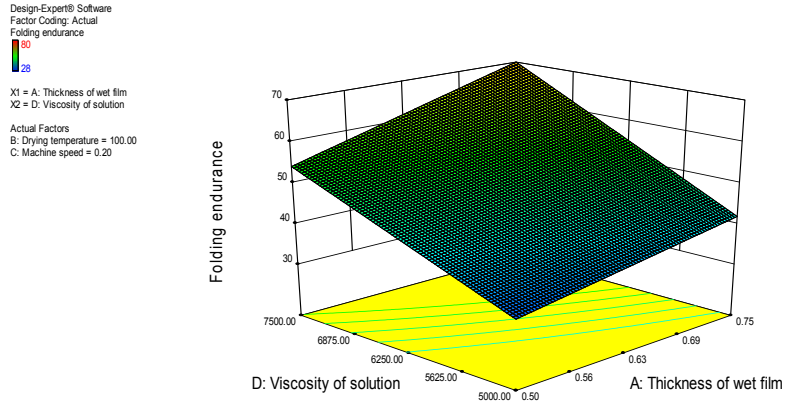

Fig. 7: Surface response plot showing the viscosity of dispersion and thickness of wet film on folding endurance of NT ODFs

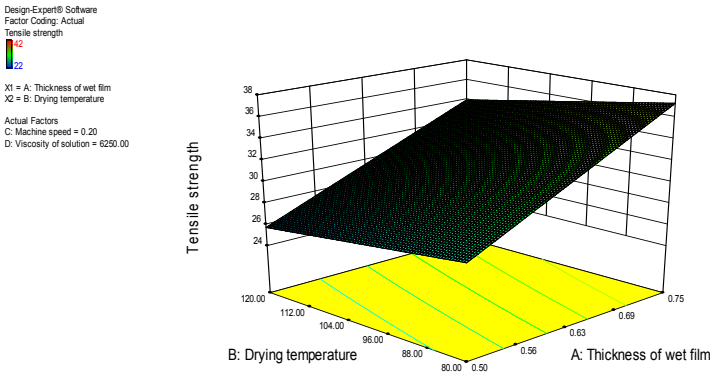

Fig. 8: Surface response plot showing the drying temperature and thickness of wet film on tensile strength of NT ODFs

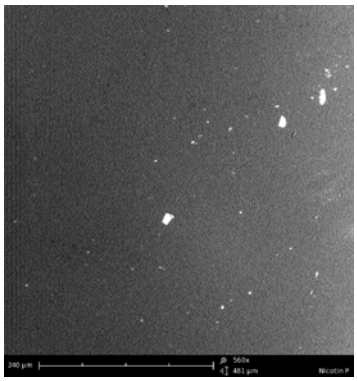

Fig. 9: Scanning electron micrograph of NT ODFs

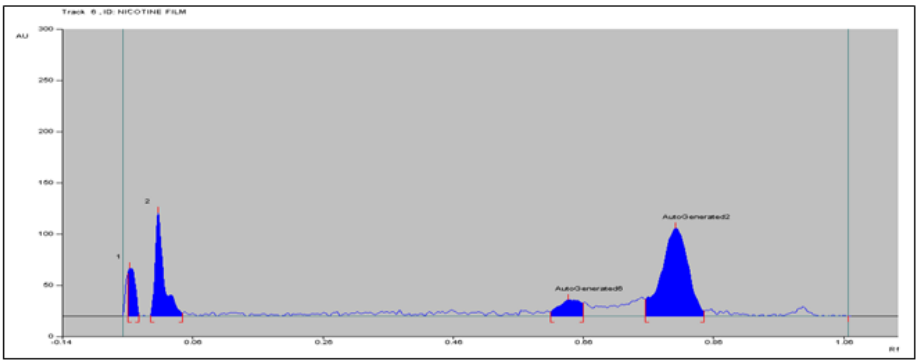

Fig. 10: Densitogram of NT extract

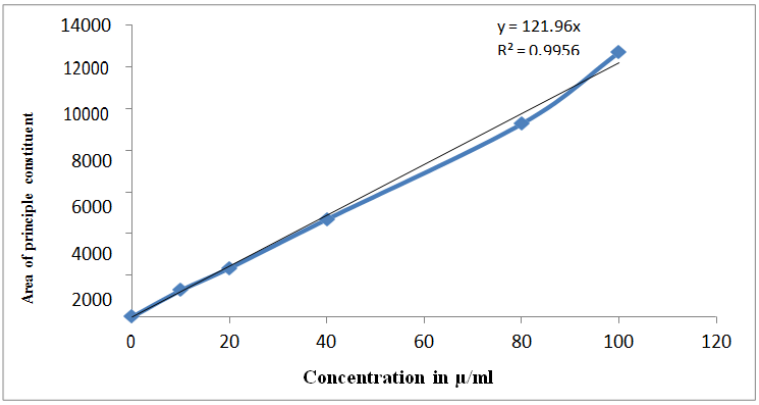

Fig. 11: Calibration curve of NT extract reference standard

Table 7: Results of microbiological limit tests for NT5 ODFs

Test	Limits	Results		
		1 mo	2 mo	3 mo
Total microbial plate count	NMT 1000 cfu/g	180 cfu/g	198 cfu/g	216 cfu/g
Total yeast and mould	NMT 100 cfu/g	20 cfu/g	18 cfu/g	24 cfu/g
Specified Micro-organism				
Escheria coli	Absent	Absent	Absent	Absent
Salmonella	Absent	Absent	Absent	Absent
Pseudomonas aeruginosa	Absent	Absent	Absent	Absent
Staphylococcus aureus	Absent	Absent	Absent	Absent

Note: cfu/g (colony forming unit/gram), NMT-Not More Than

Table 8: Organoleptic characterization of NT5 ODFs

Volunteers	Physical appearance	Taste	Bitter aftertaste
1	3	3	0
2	3	2	0
3	3	2	0
4	3	3	0
5	3	2	0
6	3	2	0
7	3	2	0
8	3	2	0
9	3	3	0
10	3	2	0
Total	30 marks	23 marks	0 marks

Table 9: Stability studies data of NT5 ODFs

Months	Physical appearance	Tack test	Disintegration time (s)		Concentration of nicotine	
			40 °C±2 °C, 75%±5%R H	30 °C±2 °C, 75%±5% RH	40 °C±2 °C, 75%±5% RH	30 °C±2 °C, 75%±5% RH
1	Translucent	Non tacky	18±0.67	19.8±0.96	99.10±1.43	99.28±1.63
3	Translucent	Non tacky	18±0.35	18.92±0.67	98.36±1.63	98.81±1.62
6	Translucent	Non tacky	18.97±0.28	20.98±0.16	98.10±0.19	98.0±0.29

Note: All the values are expressed as mean±standard deviation; n=3

Table 10: Pilot scale clinical improvement studies of NT5 ODFs

Criteria	Clinical conditions
Formulation	**Reduction in craving**
Average clinical improvement for NT5 ODFs	85.98 %
Dosage form acceptability	Yes

CONCLUSION

The aim of the present investigation was to develop and optimize NT ODFs with optimum physicomechanical and chemical properties and improved patient compliance. By controlling the thickness of wet film, the viscosity of the solution and machine speed, disintegration time, folding endurance and tensile strength of this formulation can be controlled. Therefore on the basis of these optimized values of various parameters which were obtained by applying factorial design, were prepared at a thickness (A) 0.5 mm, drying temperature (B) 80 °C, machine speed (C) 15 min and viscosity of dispersion (D) 5000 cps. The ODFs obtained using these optimized parameters were further subjected to stability and found to be stable for 6 mo. NT ODFs obtained has been accepted by patients in general and showed 85.98% reduction in craving for smoking.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Moore D, Aveyard P, Connock M, Wang D, Smith A, Barton P. Effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking: systematic review and meta-analysis. Br Med J 2009;338:1024-7.
2. Hecht SS. Tobacco smoke carcinogens and lung cancer. Cancer Inst 1991;91 Suppl 14:1194-210.
3. Siemann U. Solvent cast technology–a versatile tool for thin film production. Prog Colloid Polym Sci 2005;130:1–14.
4. Kris H, Dave V, Arnout E, Wim W, Annick L. Full factorial design, physicochemical characterization and biological assessment of cyclosporine A loaded cationic nanoparticles. Eur J Pharm Biopharm 2012;82 Suppl 1:27-35.
5. Patel R, Naik S, Patel J, Baria A. Formulation development and evaluation of mouth melting film of ondansetron. Arch Pharm Sci Res 2009;1 Suppl 2:212-7.
6. L, O'Donnell P, McGinity J. Mechanical properties of polymeric films prepared from aqueous dispersions. In: Felton ML. editors, Aqueous polymeric coatings for pharmaceutical dosage forms. 3rd edition. New York: McGraw-Hill; 2005. p. 108.
7. Fulzele SV, Sattuwar PM, Dorle AK. Polymerized rosin: novel film forming polymer for drug delivery. Int J Pharm 2002;249:175–84.
8. Shinde AJ, Garala KC, More HN. Development and characterization of transdermal therapeutics system of tramadol hydrochloride. Asian J Pharm 2008;2 Suppl 4:265–9.
9. Nishimura M, Matsuura K, Tsukioka T, Yamashita H, Inagaki N, Sugiyama T, *et al*. *In vitro* and *in vivo* characteristics of prochlorperazine oral disintegrating film. Int J Pharm 2009;368(1, Suppl 2):98–102.
10. Behin SR, Isaac SP, Fels S. Development of matrix dispersion transdermal therapeutic system containing glipizide. Pharm Lett 2013,5 Suppl 3:278-86.
11. Cilureo F, Cupone I, Minghtti P, Selmin F, Montanari L. Fast dissolving films made of maltodextrins. Eur J Pharm Biopharm 2008;70:895-900.
12. Kaushik Sunil, Khan N, Ahmad S, Singh M, Gupta S, Semwal A, *et al*. Comparative pharmacognostical evaluation and HPTLC fingerprinting of *Nicotiana tabacum* (Linn.) root collected from different geographical regions of India. Cent Eur J Exp Biol 2012;1 Suppl 1:18-25.
13. Mashru RC, Sutariya VB, Sankalia MG, Parikh PP. Development and evaluation of fast dissolving film of salbutamol sulphate. Drug Dev Ind Pharm 2005;31:25-34.
14. Sheikh S, Asghar S, Ahmad S. HPTLC method development and validation for the estimation of 6-gingerol in oral thin film. Int J Pharm Biol Sci 2013;4 Suppl 2:93-8.
15. Guidance for Industry Q1A (R2) Stability Testing of New Drug Substances and Products; 2003.
16. Liew KB, Tan YTF, Peh KK. Characterization of oral disintegrating film containing Donepezil for alzheimer disease. AAPS PharmSciTech 2012;13 Suppl 1:134-42.
17. Tingsatnd JE. Physical stability testing of pharmaceuticals. J Pharm Sci 1964;53:955-62.

18. Indian Pharmacopoeia. 6th ed. Indian Pharmacopoeia Commission. Ministry of health and family welfare, Government of India; 2008. p. 223-8.
19. Dinge A, Nagarsenkar M. Formulation and evaluation of fast dissolving films for delivery of triclosan to oral cavity. AAPS PharmaSciTech 2008;9:349-56.
20. Bruce C, Manning M. Inventor; Melt extruded thin strips containing coated pharmaceutical actives. WO 2011081625 A1; 2011.
21. Greener J, Ng KC, Vaeth KM, Smith TM. Moisture permeability through multilayered barrier films as applied to flexible OLED display. J Appl Polym Sci 2007;106:3534–42.

How to cite this article

- NGPD Nawarathna, SHT Sudeshika, HMDR Herath, DBM Wickramarathna, MHF Sakeena, CB Gunawardena. Awareness of usage of sunscreens among school children in kandy, sri lanka. Int J Pharm Pharm Sci 2016;8(8):115-123.