



Extraction and Evaluation of Linseed Mucilage as Binding Agent in Prednisolone Tablet 20 mg

Alaa Balla Suliman Abuelrakha*, Elnazeer I. Hamedelniei

¹ Faculty of Pharmacy, University of Omdurman Islamic (OIU), P.O. Box 382 Omdurman, Sudan

Article Information

Received 6 Dec 2018
Received in revised form 14 Jan 2019
Accepted 16 Jan 2019

Keywords:

Extraction
Evaluation
Linseed mucilage
Binding agent

Corresponding Author:

E-mail : alaaballa1@gmail.com
Mob.: 00249121625242

Abstract

Great interest been have develop to discover new excipients to solve problem that faced us during formulation like incompatibility and compressibility that lead to slow down manufacturing processes. Linseed mucilage has properties that suggested it as useful additives and binding agent like inertness, nontoxic and viscosity. The purpose of the present study was to extract and evaluate *linseed mucilage* as binding agent in prednisolone tablets. The Linseed mucilage was extracted and evaluated for physicochemical properties using official procedures. Tablet was prepared by wet granulation. Granules evaluation revealed satisfactory results. Three formula were prepared that contain three different percent from linseed mucilage 3%, 5% and 7%.The hardness test result show great increase in tablet hardness 4.23, 5.59 and 7.76, respectively. The dissolution test was carried in Ph 1.2 for 2 hours and cumulative drug release 20.33%, 17.88% and 14.49% respectively .And at Ph 6.8 for 4 hours cumulative drug release 78.18%, 75.43% and 69.19%. The tablets formulated showed acceptable general appearance. Formula mucilage 7% showed the best flowbility of granules, hardness and friability when compared with formulas 3% and 5%.In weight variation test indicated that the type and concentration of mucilage used were not significant. When increase the percent of mucilage in formula combined with increase in tablet hardness. Invitro dissolution study indicated that the main factors which influence the amount of drug released were the pH of the medium used and concentration of the mucilage.

1 Introduction

Solid dosage prepared with aid of suitable additives dependent on intended use and method of manufacture. Examples of excipients that can be used fillers, binders, disintegrants and lubricants¹. There are many types of binders from natural source or synthetics. Added to drug mixture to insure granules and tablets can be formed with the required strength.They can be added in the form of powder in dry granulation method or in liquid in wet granulation method it included in formulation in low concentrations typically 2%-10% by weight².

Factors related to drug or related to other additives used in the formulation or related to the binders its self influence the strength and friability of granules and tablets, example of that particles size that effect granules strength and porosity and solubility of drug and excipients in granulations solvent³ also

mechanical and film forming behaviors affect the strength and binder matrix⁴.

The application of polymers in pharmaceuticals sciences growing greatly in the field of drug delivery system and control of drug release and that because of unique properties which have not attained by other materials⁵. There are two type of polymers synthetics and natural, natural polymers have advantage of been environmental friendly processing, biodegradable, nontoxic, better patient tolerance, from edible source and low cost⁶.

Mucilage is most commonly used excipient in pharmaceutical preparations has high molecular weight, sticky and gummy substance; they are esters of sulphoric acid which is a polysaccharide⁷.There are two methods of mucilage isolations hot and cold, in cold method seed soaked in distilled water for 5

hours and then boiled for 30 min and allowed to settle, acetone was added in the same volume after marc removing to precipitate the mucilage, separated and dried in oven, sieved and stored in desiccators. Hot method plant is soaked for twelve hour in distilled water and crushed in blender for fifteen min the dispersion is boiled for thirty min and passed through eight fold muslin cloth^{8,9}.

Mucilage have a variety of application as tablet binder, disintegrant, emulsifiers, suspending agent, gelling agent, stabilizing agent, thickening agent, film forming agent, and as sustain agent in matrix tablet¹⁰.

Linseed Mucilage extracted from the seed of *Linum usitatissimum* from the family *Linaceae*, varieties grown for fibers are tall, little branched and early maturing and those for seed are not tall, more branched and high seed yield¹¹, linseed mucilage evaluated as a release retardant of drug matrix tablet in some studies¹².

Prednisolone is glucocorticoids act by inhibiting leukocyte infiltration at the site of inflammation, used for the treatment of adrenocortical insufficiency and rheumatoid arthritis¹³.

The development of new tablet binder to achieve the optimum quality of the tablet, the objective of this study starting by extracting linseed mucilage, prepare the tablet using three different concentrations of the mucilage and then tablet evaluations.

2 Materials and Methods

Materials are illustrated in table 1.

Table1: Materials used in the research

Item	Specification
Prednisolone	Gift sample from Shangahi Pharmaceutical industry
Microcrystalline cellulose	Gift sample from Azal Pharmaceutical industry
Magnesium stearate	Gift sample from Azal Pharmaceutical industry
Linseed	Purchased from local market
Aceton	Purchased from commercial market. Sudan
Talc	Gift sample from Amipharma pharmaceutical industry

All the other solvents, reagents and chemicals used were of either Pharmacopoeial or analytical grade

2.1 Extraction of linseed mucilage

The linseeds were washed with water to remove dirt's and debris, seeds were powdered and soaked in water for six hour, boiled for forty five min and left stand for one hour to allow complete release of mucilage into water, the mucilage was extracted using multilayer muslin cloth bag to remove the marc from the solution, acetone (in the volumes of three times to the

volume of filtrate) was added to precipitate the mucilage, the mucilage was separated, dried, in an oven at 40°C collected, sieved and stored¹⁴.

2.2 Physicochemical properties of mucilage

Physicochemical properties such as swelling index, pH, bulk density, tapped density, Hausners ratio, compressibility index and angle of repose were determined according to official procedures¹².

2.3 Pre-compression parameters

The powder blend was evaluated by determination of bulk density, tapped density, angle of repose, compressibility index and Hausner ratio according to the BP guidelines.

2.4 Preparation of the tablet

The tablets were prepared by wet granulation method, prednisolone, linseed mucilage and MCC were mixed together and the mixture was passed through mech(no.60), granulation was done using a sufficient amount of distilled water the wet mass passed through mesh (no.35) and mixed with magnesium stearate and talc, tablets were compressed using single rotary tablet press (lab press-1/Shakti pharmatech Pvt Ltd).

Three different formulas having different concentrations of linseed mucilage (3%, 5% and 7% w/w) were developed and total tablet weight 200mg. the composition of the designed formulations were showed in Table 2.

Table 2: Composition of the designed tablet formulation

Ingredients mg	F1 (3%)	F2 (5%)	F3 (7%)
Prednisolone	20	20	20
Linseed mucilage	6	10	14
Microcrystalline cellulose	165	161	157
Magnesium stearate	6	6	6
Talc	3	3	3
Total weight	200	200	200

2.5 Evaluation of the tablets

All tablets were evaluated for following different parameters which include¹⁵

2.5.1 General appearance

Five tablets from different batches were randomly selected and organoleptic properties such as color, odor and shape were evaluated.

2.5.2 Hardness test

Hardness indicate the ability of a tablet to withstand shocks will handling, the hardness of the tablets were determined using Erweka hardness tester, it was expressed in kg/cm², ten tablets were randomly picked from each formuland hardness of the tables wasdetermined.

2.5.3 Weight variation test

Randomly twenty tablets were selected after compression weighed individually and average was determined.

2.5.4 Friability test

Friability of the tablets was determined using Roche Friabilator. This device subjects the tablets to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Pre weighed sample of ten tablets was placed in the friabilator for 4 minutes. Tablets were de dusted using a soft wiper and re weighed.

The friability (f) is given by the formula:

$$\text{Friability (f)} = 100 (W_o - W) / W_o$$

Where W_o is weight of the tablets before the test and W is the weight of the tablet after the test.

2.5.5 Disintegration test

The disintegration test was performed in a BP Basket rack assembly using 1000ml pH 6.8 phosphate buffer maintained at $37 \pm 0.5^\circ\text{C}$.

2.5.6 Swelling index

The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of formulations F1, F2 and F3 were studied. One tablet from each formulation was kept in a Petri dish containing pH 6.8 phosphate buffer at the end of 2 h, 4 h and 6 h, kept on tissue paper and weighed and the process was continued till the end of 24 h, the percent weight gain by the tablet was calculated by formula:

$$\text{S.I} = \{(W_t - W_o) / W_o\} \times 100$$

Where; S.I = swelling index, W_t = weight of tablet at time (t), W_o = weight of tablet at time t = 0

2.5.7 In vitro drug release studies

Release of Prednisolne from the formulated tablets was studied in phosphate buffer of pH 6.8 and acidic buffer 1.2 (900ml) using a United State Pharmacopoeia (USP) 6- station Dissolution Rate Test Apparatus with a rotating paddle stirrer at 50 rpm and $37^\circ \pm 0.5^\circ\text{C}$ as prescribed for Prednisolone tablets in USP¹⁴. Prednisolone analyzed by UV spectrophotometer at 247 nm¹⁵.

3 Results and Discussion

3.1 Extraction of Linseed mucilage

The average yield of dried mucilage obtained from linseeds was 31% w/w, the mucilage obtained was yellowish brown color powder and mucilage identified by giving positive results to Rutheinium test¹⁶.

3.2 Physiochemical properties of the mucilage

The mucilage studied for its swelling behavior in distilled water in buffer in pH 6.8 and generally the swelling index calculated indicated that the mucilage can act well as binding agent¹⁷. Compressibility index, Hausner ratio and Angle of ripose showed good flowability that enhances the quality of manufacturing processes² (Table 3).

Table 3: Mucilage physiochemical properties

Parameter	Result
Swelling index in distilled water	1.8
Swelling index in pH 6.8	1.5
pH	7.2
Compressibility index	16.3%
Hausner ratio	1.17
Angle of ripose	26.5°

3.3 Pre-compression parameters

Prednisolone granules were prepared by wet granulation method using distilled water in sufficient quantity and evaluated for it physical characterization before compression. The Angle of repose results showed excellent flow, the compressibility index was found to be in the range of 10.3% to 13.8% and the Hausner ratio in the range of 1.1 to 1.16 indicating very good flowability² (Table 4).

Table 4: Pre-compression parameters

Parameters	F1	F2	F3
Angle of ripose Ø	32.4	31.5	26.7
Bulk density gm/cm ³	0.25	0.25	0.26
Tapped density gm cm ³	0.29	0.28	0.29
Compressibility index %	13.8	10.7	10.3
Hausner ratio	1.16	1.12	1.1

3.4 Evaluation of the tablets

3.4.1 General appearance

Prednisolone tablets were very pale white in color, smooth, and flat shaped in appearance.

3.4.2 Hardness test

Tablet hardness increased follows mucilage percent increasing in the formulation. Table 5 and figure 1 shows the results.

Table 5: Hardness test results

	F1	F2	F3
1	4.3	5.6	7.8
2	4.2	5.5	7.9
3	4.3	5.6	7.8
4	4.1	5.7	7.6
5	4.3	5.5	7.9
6	4.2	5.5	7.8
7	4.3	5.6	7.6
8	4.3	5.6	7.7
9	4.2	5.7	7.8
10	4.1	5.6	7.7
Mean	4.23	5.59	7.76

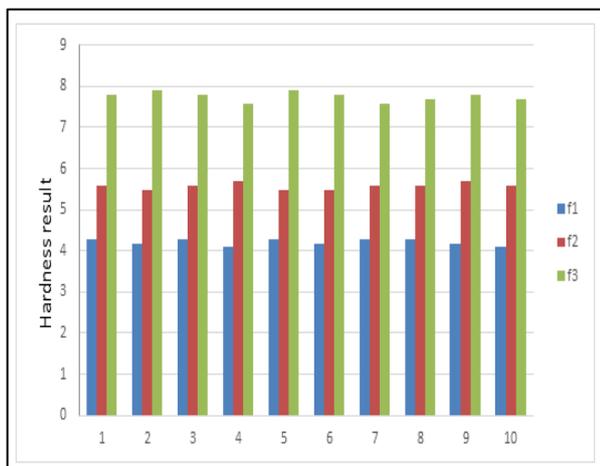


Fig 1: Tablet hardness test result

3.4.3 Weight variation

Average weight was determined and standard deviations and tablet mean calculated, none of the tablets deviated from the average weight by more than ± 5 according to USP (Table 6).

3.4.4 Friability test

Test of friability was carried in ten tablets from each formula, the result can help to predict that those tablets can withstand other manufacturing process need to be conducted¹ (Table 7).

3.4.5 Disintegration test

The tablet disintegrated took time to disintegrate but it reserved its shape as granules not turn into fine powder (Table 8).

Table 6: Weight variation result

	F ₁	F ₂	F ₃
1	205	198.8	198
2	202	197.5	205
3	197	196.2	202
4	207	198	197
5	200	202	207
6	202	197	200
7	197	204	202
8	203	197.6	197
9	198	198	203
10	202	201	198
11	195	195.6	202
12	207	203	195
13	201	200	201
14	200	197.5	201
15	198	198.2	195
16	199	201	198
17	200	198	200
18	203	197.2	203
19	198	205	199
20	199	200	200
Mean	200.65	199.28	200.15
SD*	3.18	2.62	3.13

SD: standard deviation

Table 7: Friability and disintegration test results

Formula	Friability	Disintegration
F1	0.9	15 min
F2	0.8	17 min
F3	0.6	20 min

Table 8: Percentage of release in pH 1.2

Time	F1	F2	F3
15 min	3.25	3.62	1.32
30 min	7.24	3.41	3.57
1 hour	16.17	11.27	8.35
2 hour	20.33	17.88	14.49

3.4.6 Swelling index

The swelling behavior of all formulation was studied showed the swelling characteristics of linseed mucilage containing tablets; the swelling index was calculated with respect to time, as time increases, the swelling index was increased (Fig 2).

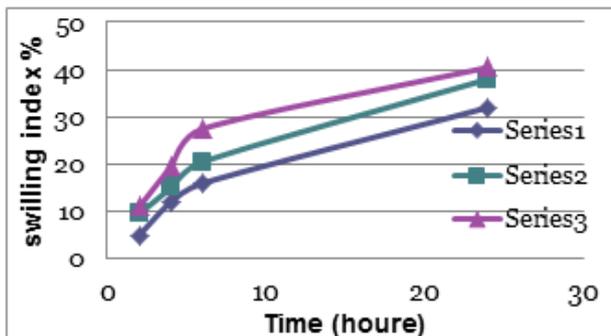


Fig 2: Tablet swelling index

3.4.7 Dissolution test result

Dissolution test results of the tablet formulated in acidic media pH1.2 showed percent of release 14.49% ,17.88% and 20.33% for f1, f2 1nd f3 respectively in dissolution time two hours. Table8 showed the percentage of release.

The dissolution behavior of the tablet in pH 6.8 presented in table 9 and Figure 3

Further studies must be conducted for different concentrations of the linseed mucilage in different pH medium and carry stability study.

4 Conclusions

The tablets formulations showed acceptable general appearance, formula mucilage 7% showed the best flowability of granules, hardness and friability when compared with formulas 3% and 5%.

In weight variation test indicated that the type and concentration of mucilage used were not significant. Increasing the percent of the mucilage in the formula lead to increase the hardness of the tablet.The tablets swelling index increased when mucilage concentrations were increased.

Table 9: Percentage of release in pH 6.8

Time	F1	F2	F3
15 min	20.86	6.92	3.57
30 min	58.24	23.19	21.18
1 hour	62.9	32.45	35.29
2 hour	66.51	46.21	50.13
3 hour	72.43	78.18	69.16
4 hour	75.43	78.18	69.19

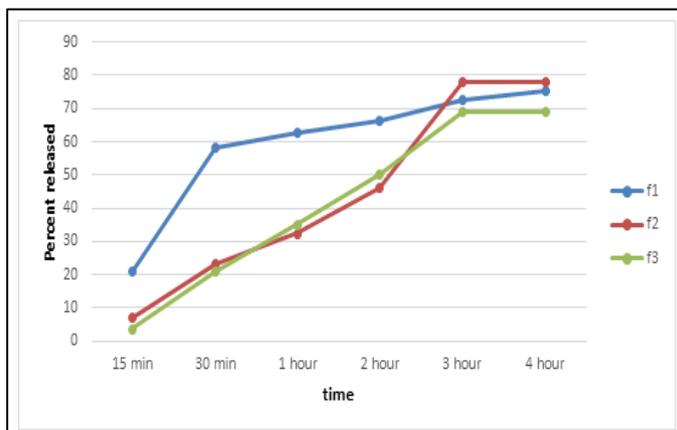


Fig 3: Percentage release at pH 6.8

5 Acknowledgement

Thanks and praise be to Allah to complete this work and prayers and peace be upon the prophet Muhammad peace be upon him.

I extend my profound gratitude to my able supervisor Dr. Elnazeer I. Hamedelniei for his support on the manner and how this research work came to be.

Sincerely my limitless gratitude goes to the family Of Omdurman Islamic University for their relentless support.

6 Competing Interests

Authors have declared that no competing interests exist.

7 Author's contributions

ABS carried out the study, interpreted the results, and prepared the manuscript. EIM participated in the design of the study and was responsible for its coordination and contributed in the preparation of the manuscript. All authors read and approved the final manuscript.

8 References

1. Allen LV, Ansel HC. Ansel's pharmaceutical dosage forms and drug delivery systems, tenth edition. 2011.
2. Aulton ME, Taylor KM. Aultons Pharmaceutics fourth addition. 2013.
3. Rowe RC. Binder substrate interaction in granulation a theoretical approach based on surface free energy and polarity. International Journal of Pharmaceutics. 1989; 52(2):149-154.
4. Thube R, Purohit S, Gothoskar A. Study of effect of custard apple pulp powder as an excipient on the properties of acetaminophen tablet. World applied sciences Journal. 2011; 12(2): 364-71.
5. James NB, Roy LW. Starch Chemistry and Technology. Third edition, 2009.

6. Deogade UM, Deshmukh VN, Sakarkar DM. Natural Gums and Mucilage's in NDDS: Applications and Recent approaches. *International Journal of PharmTech Research*. 2012; 4(2): 799-814.
7. Ameena K, Dilip C, Saraswathi R, Krishnan PN, Sanskar C, Simi S. Isolation of the mucilage from *Hibiscus rosasinensis* linn and okra (*Abelmoschus esculentus* Linn) and study of binding effects of the mucilages. *Asian Pacific Journal of Topical Medicine*. 2010;3(7):539-543
8. Senthil V, Sripreethi D. Formulation and Evaluation of paracetamol suspension from *Trigonella foenum graecum* mucilage. *Journal of Advanced Pharmacy Education and Research*. 2011;1(5):225-233
9. Jania GK, Shahb DP, Parjapati VD, Jainba VC. Gumes and mucilage versatile excipients for pharmaceutical formulation. *Asian Journal of Pharmaceutical Sciences*. 2009; 4(5): 309-323.
10. Bemiller JN, Roy LW, Davide GB, Chyi-Cheng C. Aloe, Chia , Flaxseed, Okra, Psyllium seed, Quince seed and Tamerind gumes. *Industerial Gum third edition*.1993.
11. Yadav IK, Jain AD. Formulation and Evaluation of Diclofenac Sodium Sustain Release Tablet using *Linum usitatissimum* seed mucilage matrixing. *Indian Journal of Research in Pharmacy and Biotechnology*. 2015; 3(5): 2320-3471.
12. Chauhan CS, Naruka PS, Rathore RS, Badadwal VK. Formulation and Evaluation of Prednisolone tablet for colon targeted drug delivery system. *Journal of Chemical and Pharmaceutical Research*. 2010; 2(4): 993-998.
13. Rasheed A, Uddin SA, Sultana N. Mohammed Raouf Isolation and Characterizations OF *Hibiscus Rosa Sinesis* Linn to be useful as a super disintegrant in solid oral dosage. *Indo American Journal of Pharmaceutical Research*. 2015; 5(11): 2231-6876.
14. United State Pharmacopeia 34, The National Formulary. US Pharmacopeial Convention. Washington DC: Board of Trustees publication. 2011; 2: 272.
15. British Pharmacopiea. volume III, 2016.
16. Rani K, Parvez N, Sharma PK. Extraction and Characterization of Flax seed mucilage as pharmaceutical adjuvant. *World Journal of Pharmacy and Pharmaceutical Science*. 2016; 5(7): 2278-4357.