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In Vitro - Vivo Study Of Orodispersible Tablet Of Silymarin Based Nanoparticle For Anti-Inflammatory Characterization

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ABSTRACT

Aim: The objective of this work was to enhance the anti-inflammatory properties of silymarin by developing and refining an Orodispersible tablet formulation loaded with nanoparticles.

Objective: This study report focuses on the formulation creation and optimization of an orodispersible tablet containing silymarin for its anti-inflammatory properties.

Background: By improving solubility and absorption, drug delivery methods utilizing nanoparticles can aid in overcoming these constraints. Orodispersible pills dissolve and disintegrate quickly in the mouth without the need for water, resulting in a quicker start of action.

Method: Direct compression was then used to incorporate these nanoparticles into orodispersible tablets that contained superdisintegrants and sweeteners. The tablet formulation was systematically optimized using a box-behnken design based on responses such as friability, hardness, wetting time, and disintegration time.

Result: Formulation F3, which has 5% of crospovidone as a superdisintegrant, exhibited maximum drug release, or 98.5%, after 15 minutes. The anti-inflammatory potential was assessed in rats with paw edema caused by carrageenan. After three hours, the 400 mg/kg dose showed a significant 48% inhibition; after three hours, the impact rose to 52%.

Conclusion: Overall, the creation of orodispersible silymarin nanoparticle tablets holds out hope for enhancing silymarin's anti-inflammatory properties through the complementary use of fast-dissolving tablet and nanoencapsulation technologies.

Keywords: *Orodispersible tablets, rapid dissolving, rapid disintegration, anti-inflammatory acticity, nanoparticles.*

1. INTRODUCTION

A significant field of pharmaceutical research that seeks to improve the bioavailability and therapeutic efficacy of active medicinal molecules is the creation of innovative drug delivery systems. One such method that is attracting a lot of attention is nanoparticle-based delivery, which encapsulates drug molecules in very small carrier particles that are in the nanosize range. Milk thistle is the source of silymarin, a bioactive flavonoid molecule with low oral bioavailability and aqueous solubility. Polymeric nanoparticle encapsulation of silymarin may be able to get around these restrictions by boosting absorption, enhancing solubility, and shielding the medication from deterioration. In order to improve oral administration, the formulation and optimization of silymarin-loaded nanoparticle orodispersible tablets is the main goal of this research. [1-4]

Orodispersible pills are easy to administer since they dissolve quickly in the mouth without the need for water. It might be feasible to create a delivery strategy that optimizes silymarin absorption and the ensuing therapeutic effects by mixing nanoparticles with orodispersible tablets. Silymarin has hepatoprotective, antioxidant, and anti-inflammatory qualities that make it a potential treatment for a number of ailments. In order to create orodispersible tablets with the right hardness and disintegration time, tablet excipients will also be tuned. The overall goal of this project is to create a new orodispersible tablet formulation of silymarin based on nanoparticles that has improved oral bioavailability for potent anti-inflammatory treatment. [5-7]

The terms mouth-dissolving, melt-in-mouth, fast-dissolving, rapid-melt, porous, and quick- dissolving are other terms for orodispersible tablets. They have the special ability to dissolve and release the medication quickly when they come into contact with saliva, negating the need for water during administration. They also transform into a soft paste or liquid form that is easy to swallow and poses no choking hazard. [8–12]

2. MATERIAL AND METHODS

- **Materials:**

Silymarin (Strides Arco lab Limited, Bangalore), Eudragit® -EPO (Cipla Pharmaceuticals, Mumbai , India.), Pluronic F-68 (Alembic Pharmaceuticals, Mumbai.), Chloroform (Loba Chemie pvt ltd., Mumbai), Hydrochloric Acid (Sd fine-Chem. Limited, Mumbai.), Diethyl ether (Loba Chemie pvt ltd., Mumbai), Disodium hydrogen phosphate (Sd fine-Chem. Limited, Mumbai.),

- **Preparation of Tablets:**

The Direct Compression technique was used in this work to prepare the orodispersible tablets.

When compared to the wet granulation approach, direct compression in tableting needs fewer processing stages, is easier to validate, and improves medication stability. In addition to being a more cost-effective method, direct compression also removes processing exposure to heat and moisture.Filler that is directly compressible need to have good compactibility and flowability. While high compactibility is required to create tablets with enough mechanical strength, good flowability is required to guarantee quick and consistent die filling. [15–17]

Table 1: Formulation of Tablets

Ingredients	**F1 mg**	**F2 mg**	**F3 mg**	**F4 mg**	**F5 mg**	**F6 mg**	**F7 mg**	**F8 mg**	**F9 mg**
SL-NP	26.4	26.4	26.4	26.4	26.4	26.4	26.4	26.4	26.4
SSG	-	-	-	-	-	-	1.5	2.7	4.5
CCS	-	-	-	1.5	2.7	4.5	-	-	-
CP	1.5	2.7	4.5	-	-	-	-	-	-
Mannitol	19.2	18.3	16.5	19.2	18.3	16.5	19.2	18.3	16.5
Aspartame	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
Flavoring agent	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
MS	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Talc Powder	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Total weight	50	50	50	50	50	50	50	50	50

SL-NP: Silymarin-nanoparticles, SSG:Sodiumstarchglycolate, CCS:Croscarmelose sodium, CP-Crosspovidone

- **Pre-compression studies on powder blend: [18-19]**
  - **Bulk density: The bulk density was discovered to be between 0.5 and 0.522 g/ml.**
  - **Tapped density: Between 0.583 and 0.598 g/cm3 was the range of the tapped density.**
  - **Compressibility index: Compressibility index values under 15% indicate acceptable flow, whereas values over 15% suggest poor flow characteristics. [16-20]**
  - **Hausner ratio: Good flow properties are indicated by a lower Hausner ratio, or <1.25, as opposed to a greater Hausner ratio, or >1.25.**
  - **Angle of repose (θ): The results fall within the range of 21.8 to 23.270, indicating that the powders have good flow properties.**

Table 2: Pre compression study of all formulations

Batch	Bulk density* g/ml ±0.15	Tapped density* g/cm	Compressibility Index*	Hausner ratio*	Angle of repose (θ)*	Average weight variation*	Hardness* (Kg/cm2)	Thickness* (mm)	Friability* (%)
F1	0.53	0.62	12.35	1.14	22.5	454	3.20	5.13	0.44
F2	0.51	0.6	13.40	1.13	24.7	451	3.30	5.46	0.46
F3	0.57	0.65	12.48	1.06	25.9	449	3.30	5.72	0.44
F4	0.54	0.62	13.40	1.13	24.6	449	3.13	5.27	0.49
F5	0.62	0.69	12.50	1.13	23.5	455	3.20	5.29	0.46
F6	0.58	0.66	13.36	1.10	26.3	453	3.33	5.35	0.46
F7	0.54	0.61	13.46	1.16	24.2	452	3.26	5.58	0.47
F8	0.52	0.59	13.5	1.14	25.4	454	3.36	5.71	0.44
F9	0.59	0.68	13.26	1.18	26.3	452	3.40	5.65	0.46

- **Post Compression Studies: [20-26]**
  - **Weight variation:** Tablets that have been prepared were assessed for weight variance.
  - **Hardness:** The tablets' hardness was determined to be between 3.13 and 3.4 kg/cm2, which is adequate to withstand mechanical shocks from handling during production, packing, and shipment.
  - **Thickness:** The tablet's thickness was determined to be between 5.13 and 5.72 mm, which is enough for packing and acceptance.
  - **Friability:** The tablet's friability was discovered to be between 0.447 and 0.493%. The numbers are less than one percent, which is the official monograph's limit.
  - **Rapidly disintegrating property:** [21-26]
  - **Wetting time:** All the superdisintegrants were found to have good hydrophilicity, as shown by the values, which were determined to be between 29 and 41.6 seconds.
  - **Modified disintegration test:** The adjusted disintegration times of the several formulations were shown, and the results fall between 34 and 43.6 seconds**.**
  - **Water absorption ratio:** The findings fall between 25.31 and 29.2.
  - **In Vitro dispersion time:** The time required for uniform dispersion is used to calculate the In- Vitro dispersion time. The results fall between 62 and 77 seconds.
  - **In Vitro drug release:** Several formulations' in vitro release was investigated and is displayed in the table. At the conclusion of 15 minutes, the drug release of formulations F1 through F9 is 94.7%, 95.6%, 99.5%, 91.9%, 94.2%, 96.4%, 90.0%, 92.6%, and 94.8% of silymarin,

respectively. The quick absorption and tablet disintegration into small particles may be the cause of the formulations' quick dissolving. As a result, after 15 minutes, formulation F3 displayed maximum drug release, or 98.5%.

  - **Drug content:** The range of content homogeneity and the proportion of drug content in different formulations are 99.16 to 99.88 percent.
  - **Stability study:** For a month, the formulation F3 was maintained in a stability chamber at 40±20C and 75±5% relative humidity for an expedited stability investigation.

Table 3: Rapidly disintegrating property of all formulations

Batch	Wetting time* (Sec)	Disintegration time* (sec)	Water absorption ratio*	Dispersion time* (sec)	Drug content (%)
F1	38.0	41.0	25.31	73.3	99.56±0.54
F2	34.6	40.3	26.46	70.3	99.72±0.63
F3	29.0	34.0	29.0	62.0	99.88±0.58
F4	34.6	43.6	26.18	77.0	99.16±0.51
F5	41.3	42.6	26.30	67.3	99.45±0.62
F6	33.3	37.6	27.22	64.0	99.61±0.69
F7	41.6	43.3	26.20	76.0	99.29±0.43
F8	37.0	39.6	27.01	72.0	99.48±0.58
F9	33.3	38.3	29.20	67.6	99.57±0.66

- **In Vitro drug release:** The quick absorption and tablet disintegration into small particles may be the cause of the formulations' quick dissolving. As a result, after 15 minutes, formulation F3 displayed maximum drug release, or 98.5%.

Table 4: In Vitro % drug release

Batch	% drug release				
	3 (min)	6 (min)	9 (min)	12 (min)	15 (min)
F1	64.3	71.8	80.5	87.6	94.7
F2	66.5	72.0	79.1	86.2	95.6
F3	69.6	72.0	78.3	89.4	99.5
F4	68.0	71.7	78.0	85.6	91.9
F5	69.7	73.4	79.0	87.0	94.2
F6	68.2	71.0	76.3	88.2	96.4
F7	65.1	70.1	76.4	84.5	90.0
F8	67.3	72.0	79.0	86.5	92.6
F9	68.1	74.5	79.6	88.9	94.8

- **Animal studies**
  - **Approval**

The Institutional Animal Ethics Committee (IAEC) clearance number IAEC:1877/PO/Re/s/16/CCSEA/2023/002 and the Committee for the Purpose of Control and Supervision of Experiments on Animals (CCSEA) gave their consent for the study to be carried out.

- **Anti-Inflammatory Activity of Silymarin Loaded Nanoparticles**

For this investigation, 20–25 gm Swiss albino mice and 150–200 gm wistar rats were employed. The creatures came from an animal shelter. When the animals arrived, they were divided into treatment groups and put in polypropylene cages with

bedding made of rice husk at random. The animals were kept in rooms with a 24±2ºC temperature and a 30–70% relative humidity. A12: The day cycle was adhered to animals [27-30]

- **Stability study:** For a month, the formulation F3 was maintained in a stability chamber at 40±20C and 75±5% relative humidity for an expedited stability investigation. The samples were checked for any changes in physical parameters after a two-month period. There was no discernible change in the flavor or color of the tablets, and there was no unpleasant smell.

Table 5: Evaluation parameters obtained after stability study of the Silymarin ODT (2 months)

S. No	Parameters	Units	F3 (Days)			
			15	30	45	60
1	Hardness	Kg / cm^2	3.30±0.41	3.28±0.35	3.25±0.45	3.24±0.28
2	Friability	% w/w	0.44±0.38	0.45±0.25	0.43±0.41	0.42±0.32
3	Disintegration time	Sec	35.0±0.4	34.6±0.2	34.1±0.5	33.4±0.2
4	Wetting time	Sec	28.0±1.8	27.3±0.3	26.8±0.1	26.3±0.3
5	Assay	%	99.88±0.5	99.54±0.7	99.20±0.3	98.8±0.4

- **Anti-Inflammatory Activity -Carrageenan-Induced Paw Edema in Rats.**

The Table displays the anti-inflammatory impact of Silymarin Loaded Nanoparticles on carrageenan-induced hind paw edema. At 200 and 400 mg/kg, the Silymarin Loaded Nanoparticles significantly reduced the inflammatory effects caused by carrageenan. After three hours, the 400 mg/kg dose showed a strong 48% inhibition; after three hours, the impact grew to 52%. Silymarin-loaded nanoparticles had a notable and comparable anti-inflammatory effect to that of diclofenac sodium (10 mg/kg).**Error! Reference source not found.**

Table 6: Anti-inflammatory activity of Silymarin Loaded Nanoparticles on Carrageenan induced paw edema method in Wistar rats

GROUP	Paw thickness in mm					% Inhibition at 3hr
	0 hr	1hr	2hr	3hr	4hr	
Group-I Carrageenan (control)	1.4	3.4	4.9	6.4	4.8	------
Group-II D.S. (10mg/kg)	1.4	2.2	2.9	3.1	2.2	52
Group-III (200mg/kg of SL-NP)	1.2	3.0	4.2	4.7	3.5	27
Group-IV (400mg/kg of SL-NP)	1.1	2.7	3.5	3.3	2.8	48

D.S.Diclofenac Sodium ,Values were mean ± SEM, (n=6), **P*<0.05, ***P*<0.01 Vs control SL-NP= Silymarin Loaded Nanoparticles

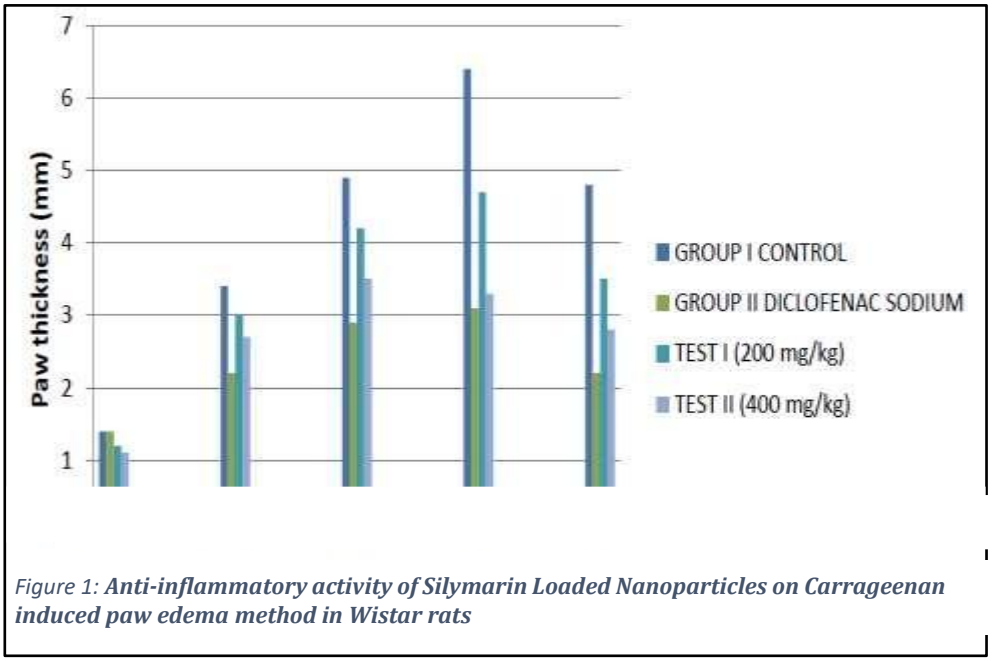

Figure 1: ***Anti-inflammatory activity of Silymarin Loaded Nanoparticles on Carrageenan induced paw edema method in Wistar rats***

Data were analyzed by using One-way ANOVA followed by Dunnett's test

3. CONCLUSION

Because they are more patient-friendly orodispersible dose forms have the potential to improve the safety, acceptability, and efficacy of pediatric pharmacotherapy. However, a number of drawbacks that could not have been resolved by traditional formulation methods have impeded their development, including the unique pharmacokinetic and biopharmaceutical properties of the active ingredients as well as their organoleptic profile. Although nanostructures have primarily been studied as injectable drug carriers for the treatment of tumors, the wide range of materials that can be used to prepare them can make them useful for oral pharmacotherapy. This is because many of the drawbacks of oral and orodispersible medication can be easily addressed by incorporating them into various nanostructures.

REFERENCES

[1] Tejvir Kaur, Bhavandeep Gill, Sandeep Kumar, G.D.Gupta;,Mouth dissoving tablets: A novel approach to drug delivery; International Journal of Pharmaceutical Research, 2011,vol 3, issue 1,1-7.

[2] Md.Nehal Siddiqui, Garima Garg,Pramod Kumar Sharma;,Fast dissolving tablets: Preparation, characterization and evaluation: over view; International Journal of Pharmaceutical Sciences Review and Research, 2010,sept-oct, vol 4, issue 2, article 015, 87-96.

[3] Jaysukh J Hirani, Dhaval A Rathod, Kantilal R Vadalia;,A review on orally disintegrating tablets; Tropical Journal of Pharmaceutical Research, 2009,April, vol 8, issue 2, 161-172.

[4] S Furtado, R Deveswaran, S Bharath, B V Basavaraj, S Abraham, V Madhavan;, Development and characterization of orodispersible tablets of famotidine containing a subliming agent; Tropical Journal of Pharmaceutical Research, 2008,December, vol 7, issue 4, 1185-1189.

[5] Patel Bipin, Dr.J.K.Patel, Rajput Ganesh, Thakor Rashmin;,formulation and evaluation of mouth dissolving tablets of cinnarizine; Journal of Pharmacy Research, march, 2009, vol 2, issue 3, 510- 513.

[6] Vijay Tiwari, Dhana jay kinikar, Krishna Pillai, P.D.Gokulan;,Preparation and evaluation of fast dissolving tablets of celecoxib; Journal of Current Pharmaceutical Research, 2010, vol 04, 4-11.

[7] Ashwini R.Madgulkar, Mangesh R.Bhalekar, Rahul R.Padalkar;,Formulation and optimization of novel taste masked mouth dissolving tablets of tramadol having adequate mechanical strength; American Association of Pharmaceutical Scientists PharmSci Tech, 2009,june, vol 10, no. 2, 574- 581.

[8] Sachin B.Mahamuni, Sadhana R.Shahi, Nandakishor V.Shinde, Gaurav R.Agarwal;,Formulation and evaluation of fast dissolving tablets of promethazine hcl with masked bitter taste; International Journal of Pharmaceutical Research and Development, 2009,sept, vol 7, 1-18.

[9] Vineet Bharadwaj, Mayank Bansal, P.K.Sharma;,Formulation and evaluation of fast dissolving tablets of amlodipine besylate using different superdisintegrants and camphor as sublimating agent; American-Eurasian

Journal of Scientific Research, 2010, vol 5, issue 4, 264-269.

[10] Ronald J. Neufeld., Catarina Pinto Reis., Antonio J. Ribeiro and Francisco Veiga.,Nanoencapsulation methods for preparation of drug-loaded polymeric nanoparticles. Nanotechnology, Biology and Medicine, 2006, 2, 8-21.

[11] Pushpendra Goswami and Shilpa Subhedar,Nanotechnology: Role and Future Trends in Pharmacy. Journal of Pharmacy Research, 2011, 4(11), 4021-4024.

[12] Gadad A., Soni A., Dandagi P and Mastiholimath V. Nanotechnology in drug delivery- A Review. Indian Drugs, 2011, 48 (11), 5-15.

[13] Behera A. L., Patil S. V., Sahoo S. K and Sahoo S. K.,Nanosizing of drugs: A promising approach for drug delivery. Der Pharmacia Sinica, 2010, 1 (1), 20-28.

[14] Mohanraj V. J and Chen Y.,Nanoparticles – A Review. Tropical Journal of Pharmaceutical Research, 2006, 5 (1), 561-573.

[15] Metker Vishal, Kumar Anju, Pathak Naveen, Padhee Kumud, Sahoo Sangram;,Formulation and evaluation of orodispersible tablets of lornoxicam; International Journal of Drug Development and Research, 2011,jan-march, vol 3, issue 1, 281-285.

[16] S Furtado, R Deveswaran, S Bharath, B V Basavaraj, S Abraham, V Madhavan;,Development and characterization of orodispersible tablets of famotidine containing a subliming agent; Tropical Journal of Pharmaceutical Research, December, 2008,vol 7, issue 4, 1185-1189.

[17] Jyoti Singh, Meenakshi Bajpai;,Effect of superdisintegrants in the formulation of taste-masked orodispersible tablets of tizanidine HCl; Journal of Pharmacy Research, 2011, vol 4, issue 7, 2175- 2178.

[18] Sunil H.Makwana, Dr.L.D.Patel, Tejas B.Patel, Tushar R.Patel;,Formulation and evaluation of taste masked orodispersible tablets of ondansetron hydrochloride; Journal of Pharmaceutical Sciences and Research, 2010, vol 2, issue 4, 232-239.

[19] Dharmajit Pattanayak, Saumya Das, Pritosh Pattanaik;,Formulation and evaluation of norfloxacin orodispersible tablets; International Journalof Pharma World Research, 2010,jun-sept, vol 1, issue 3, 1-11.

[20] Shid S.L, Hiremath S.P,Borkar SN, Sawant VA, Shende VS, Tote MV, Birari R.B, Changrani S.R;,Effect of superdisintegrants in rapidly disintegrating flurbiprofen sodium orodispersible tablets via direct compression and camphor sublimation; Journal of Global Pharma Technology, 2010, vol 2, issue 1, 107-117.

[21] Lachman L., Liebermann A., Herbert K and Joseph L. The theory and practice of Industrial Pharmacy, 3rd edition, Varghese Publishing House Mumbai,; 1991,293- 373.

[22] Anonymous. Indian Pharmacopoeia. 7 th edn.,, Government of India, Ministry of Health and Family Welfare, The Indian Pharmacopoeial commission, Ghaziabad,; 2014,vol. 1 &2,185,1722- 1724.

[23] Anonymous, The United States Pharmacopoeia XXXII, NF XXVII. The United States Pharmacopoeial convention, Rockville, MD, USA. Volume I, 2009; 1101, 1192.

[24] Goodman and Gillman's.,The Pharmacological Basis of Therapeutics Mc Graw-Hill Medical Publishing Division, New York,; 2008,853-908.

[25] Sweetman S.C., Martindale The Complete drug reference, 36th edn., The Pharmaceutical press, London,; 2009,718.

[26] Anonymous. Indian Pharmacopoeia. 5 th edn.,, Government of India, Ministry of Health and Family Welfare, The Indian Pharmacopoeial commission, Ghaziabad,; 2014,496-500.

[27] Safari VZ, Ngugi MP, Orinda G and Njagi EM.:Anti-pyretic, anti- inflammatory and analgesic activities of aqueous leaf extract of Urtica dioica L. in albino mice. Medicinal and Aromatic Plants. 2016,5(2):1-7.

[28] Al-khazraji SM. Studying the Analgesic, Anti-inflammatory and Antipyretic Properties of The Aqueous Extract of Petroselinum crispum in Experimental Animal Models. *IOSR Journal of Pharmacy*: 2015,9: 17- 23.

[29] Kumar S, Vandana UK, Agrwal D and Hansa J. Analgesic, anti- inflammatory and anti-pyretic effects of Azadirachta indica (Neem) leaf extract in albino rats. *International Journal and Science Research*.: 2015,4:713-21.

[30] Onasanwo SA, Fabiyi TD, Oluwole FS and Olaleye SB. Analgesic and anti-inflammatory properties of the leaf extracts of Anacardium occidentalis in the laboratory rodents. Niger. J. Physiol. Sci.: 2012, 27:65- 71.