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FORMULATION AND EVALUATION OF SEMI- INTERPENETRATING POLYMER NETWORK MICROSPHERES OF ANTIANGINAL DRUG USING *DELONIX REGIA* GUM

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ABSTRACT

The goal of the current project is to develop semi-IPN microspheres of Nicorandil using Chitosan and delonix regia gum by emulsion cross-linking method. Nicorandil was chosen as a model drug. DRG-Semi-IPN microspheres were prepared at varying speed from which 3000rpm was found to be optimum. The drug was loaded into beads by varying their composition such as, amount of crosslinker glutaraldehyde and ratio of chitosan. Glutaraldehyde was used as a cross-linker at varying concentrations 2,4,6ml in which 4 ml was selected as optimum. A total of nine batches were prepared by varying the polymer blend ratio and by using glutaraldehyde as a cross-linking agent. The prepared microspheres were subjected for various evaluation parameters such as Drug content, % Entrapment efficiency, Swelling behavior, and in-vitro release study. From the results, batch F5 was selected as the optimized batch as it showed 94.55% drug release, and 87.0% entrapment efficiency, and the optimized batch was evaluated using FTIR, SEM, and stability study. The stability studies were carried out on optimized formulation F5 at 400 C± 20 C and 75% ± 5% RH for three months. The microspheres were evaluated for percent drug loading, percent drug entrapment efficiency and percent cumulative drug release for 0, 30, 60, and 90 days. No significant changes in percent drug loading, percent drug entrapment efficiency, and drug release were obtained and hence it was concluded that the optimized batch (F5) was stable.

KEYWORDS: Delonix Regia seeds (DRG), Antianginal drug, Microspheres, Natural Polymers, Nicorandil.

INTRODUCTION

Oral drug delivery system is known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms.[1]

The formulations for continuous release and regulated release have become very popular. The conventional dose formulas are swiftly replaced by these state-of-the-art, controlled release techniques. Drug delivery systems classified as sustained-release, prolonged-release, modified-release, extended-release, or depot formulations aim to attain or prolong therapeutic effect by continuously releasing medication over an extended period of time following administration of a single dose. "Any drug or dosage form or prescription that prolongs the therapeutic activity of the drug" is the most basic definition of sustained release. The primary objective is to deliver the drug into the body at a predefined pace for the designated duration after injecting, implanting, or consuming the drug orally.[2] The high amount of DRG increases hydrophilicity leading to formation of viscous gel structure with water which may have blocked the pores on the surface of microspheres and sustained the release profile of drug.

The chemical crosslinking method for preparation of chitosan microspheres involves emulsification followed by crosslinking with a suitable crosslinking agent (e.g., GA). Chitosan microspheres have been prepared by emulsion crosslinking, ion-induced coagulation, and spray drying methods. Of these methods, the most common method used to prepare chitosan microspheres is the emulsion chemical crosslinking method.[3]

Nicorandil is a Selective ATP dependent potassium channel opener which as used as prevention and treatment of chronic stable angina (sensation of pressure, squeezing or pain in the chest due to Insufficient the blood to the muscles of the heart) and acute Coronary syndrome.[4] In the present investigation, the performance of Semi-IPN microspheres of DRG and sodium Chitosan, prepared by emulsion cross linking technique,

was evaluated. Taking into account above-mentioned aspects of Nicorandil, it was decided to use Nicorandil as a model drug. The prepared Semi- IPN micropheres were optimized and evaluated.

MATERIAL AND METHOD

Nicorandil was obtained as a gift sample from Supriya lifescience ltd pharmaceuticals, Lote Parshuram Industrial Area, MIDC, Tal.khad, Dist. Ratnagiri, India. Delonix Regia Seeds Rajesh nursery & seeds store 377, Indra nagar colony, P.O. new forest, DEHRADUN 248006 (Uttarakhand). Glutaraldehyde, Potassium Dihydrogen phosphate, Hydrochloric Acid Sodium Hydroxide and Light liquid paraffin were procured from Loba chemie Pvt. Ltd. All other chemicals and ingredients used in the study were of analytical grade.

Isolation and purification of DRG[5]

Fig no.1: Pictorial representation of DRG.

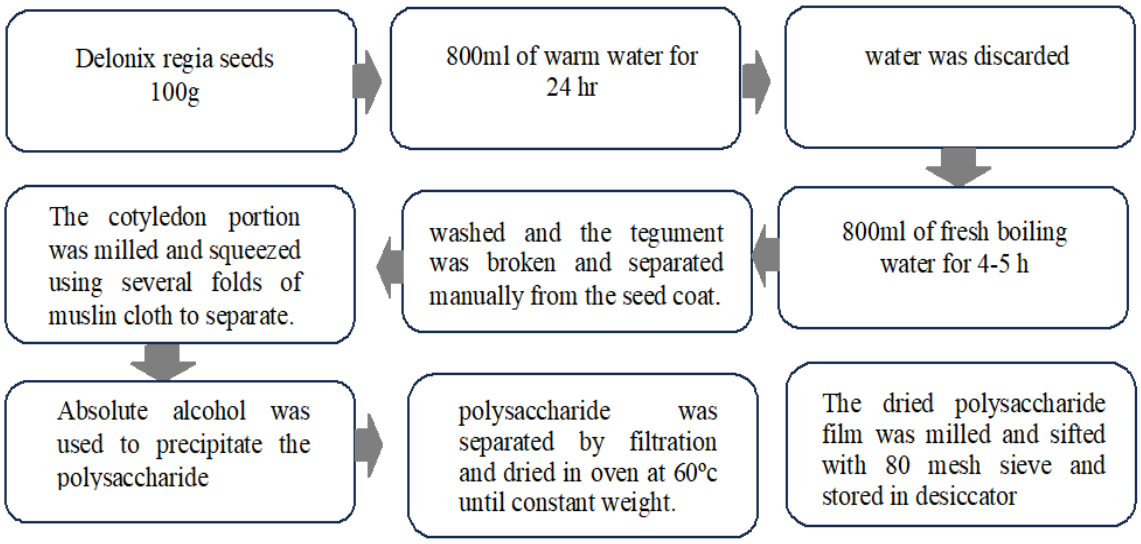

Fig.no.2 Diagrammatic representation of isolation and purification of DRG.

Characterization of drug, polymer by Fourier Transform Infrared Spectroscopy

Fourier transform spectroscopy is an important technique applicable for identification of functional groups present in a compound. The weighed quantity of sample was blended with solid Kbr powder. This physical mixture was compressed and converted into pellet then placed in the scanning slot of FTIR and subjected to FTIR spectroscopy. Transmitances were recorded at wave number between 4000and 400cm-1.

Preparation of semi-IPN microspheres[6][4][7]

The semi-IPN microspheres composed of different ratio of Delonix regia gum: chitosan containing Nicorandil were prepared by emulsion cross-linking method. Briefly, Delonix regia gum was dissolved in water by continuous stirring until a homogenous solution was obtained. After this, different ratio of DRG was dispersed in different ratio of chitosan. Nicorandil was added to above polymeric dispersion. This mixture was slowly added to 100ml light liquid paraffin containing 1% span 80 under constant stirring for 10 min. A milky white emulsion was formed. To this w/o emulsion, after 10 & 40 min, glutaraldehyde containing 0.5ml of 1N HCL was added and stirring was continued fo 3 hour. Suspension of methacrylic acid & DRG microspheres in paraffin oil, thus obtained was allowed to stand for 15 min to let the microspheres settle down under gravity. The hardened microspheres were poured in petri plate and washed with acetone & n-hexane to remove oil. The microspheres were dried at 40°c for 24 hour and stored in desiccator until further use. Total nine batches were prepared as per formulation codes.

Table No. 1: Composition of semi-IPN microsphere.

Batches	Nicorandil(mg)	Delonix regia (% w/v)	Chitosan (% w/v)	Glutaraldehyde (ml)
F1	200	1	1	2
F2	200	2	1	2
F3	200	3	1	2
F4	200	1	1	4
F5	200	2	1	4
F6	200	3	1	4
F7	200	1	1	6
F8	200	2	1	6
F9	200	3	1	6

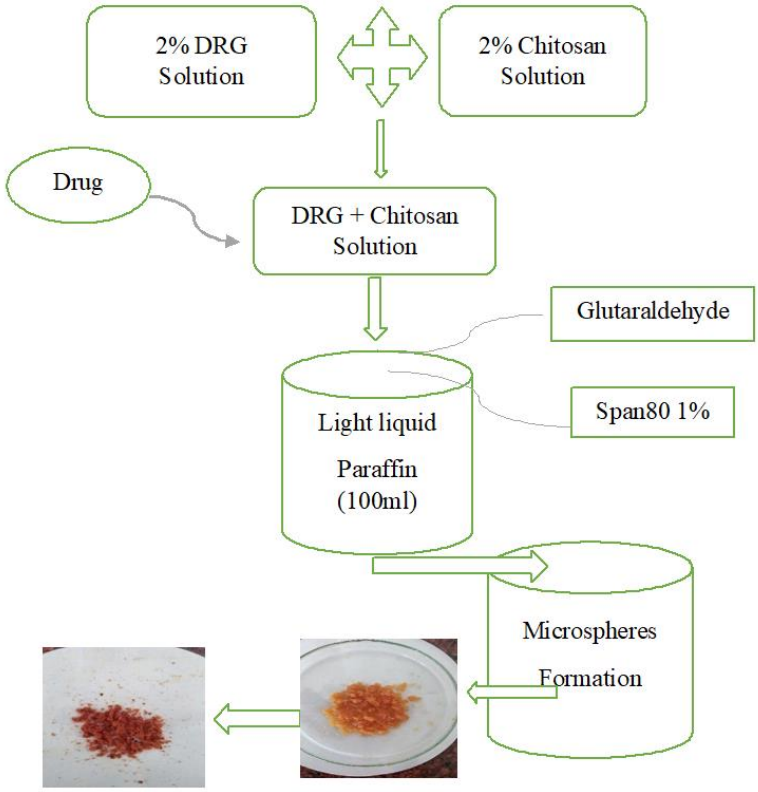

Fig no.3: Schematic representation of preparation of semi-IPN microspheres.

EVALUATION OF SEMI-IPN MICROSPHERES

1. Drug content and entrapment efficiency[4]

Precisely weighed 25 mg microspheres were broken up and distributed in 100 ml of pH 6.8 phosphate buffer, followed by a 20-minute sonication. The mixture was swirled for six hours using a magnetic stirrer. After filtering the dispersion, the drug content was measured at 263.60 nm using spectrophotometry. The following formula was used to determine the % Drug Entrapment Efficiency:

$$\% \text{ Drug Entrapment Efficiency} = \frac{\text{Practical drug content}}{\text{Theoretical drug content}} \times 100$$

2. Particle Size Analysis[8]

At least 100 microspheres from each batch were counted by placing the microparticles on a glass slide for particle size analysis, and the mean particle size was determined. The imaging system (Metzger optical instrument) equipped with a camera was used to perform the particle size analysis of the prepared IPN microspheres.

3. Swelling study[5]

Cross-linked microspheres loaded with nicotinamide were tested for water uptake in solutions of phosphate buffer 6.8 and acid buffer pH 1.2. Microspheres were let to swell for two hours in a pH 1.2 buffer solution and subsequently in a pH 6.8 solution for ten hours. Soft tissue paper was used to remove any extra adhesive liquid droplets, and an electronic balance was used to

weigh the microspheres with an accuracy of ±0.01 mg. The microspheres were baked at 60 degrees Celsius for five hours, or until the sample's dried mass remained unchanged.

$$\text{Swelling Index (\%)} = \frac{\text{Weight of microspheres after swelling} - \text{Dry weight of microphores}}{\text{Dry weight of microphores}} \times 100$$

4. In vitro dissolution study[9]

Dissolution Test Apparatus (Model No. DA-3 Veego Scientific Devices, Mumbai) was the USP Type I (Basket Method) apparatus used for the in vitro dissolution investigation. Two dissolving media, phosphate buffer solution pH 6.8 and acid buffer pH 1.2, were employed in succession to replicate the pH variations along the GI tract. 200 mg of the formulation, weighed, was placed in a muslin cloth and submerged in 500 ml of dissolving medium in acid buffer pH 1.2 for the initial two hours, then in phosphate buffer solution pH 6.8 for the remaining ten hours. The temperature was set at $37^0C \pm 0.5^0C$ and the speed was kept at 100 rpm. A single milliliter of the aliquot sample was taken during the dissolution study at intervals of sixty minutes to twelve hours, and it was replaced with an equivalent volume of fresh medium. The withdrawn samples were filtered through Whatmann filter paper no.42 and volume make up to 10 ml with suitable buffer. The withdrawn samples were analyzed at 261.80 nm and 263.60 nm, by double beam UV visible spectrophotometer and percent cumulative release was calculated.

5. Characterization of optimized formulation

1. FTIR Study of Optimized formulation[9]

Potassium bromide and Optimized Formulation (Batch F5) were thoroughly combined. This physical mixture was formed into a circular disc by compression. After that, the disk was inserted into the FTIR scanning slot and scanned within the 40–4000cm-1 range.

2. Scanning Electron Microscopy[5]

Particle size distribution, surface morphology, and shape were all determined by scanning electron microscopy. At the University of Technology, Osmania University, Hyderabad, the dry microspheres were placed on the brass stub and observed under an analytical scanning electron microscope (SEM) equipped with a Hitachi, Japan model number S-3700N.

6. Stability Study[10]

Formulation F5 was retained for the stability investigation after it was determined to be the optimal formulation due to its desirable qualities. An optimized formulation's stability was investigated by keeping the microspheres—wrapped in aluminium foil—for three months at 40 ± 2 ^{0}C and 75 ± 5% relative humidity. The microspheres were tested for drug loading percentage, entrapment efficiency percentage, and in vitro release data every month.

RESULT AND DISSUSSION

In the present study Nicorandil loaded semi-IPN microspheres were prepared by emulsion cross-linking with glutaraldehyde using chitosan as a cross-linking polymer and Delonix regia gum as a neutral polymer. Delonix regia gum in different concentration were selected for the formulation of microspheres is shown in Table No.1. Microspheres prepared at varying speed from which 3000rpm was found to be optimum and similarly, glutaraldehyde was used as a cross-linker at varying concentration 2,4,6ml in which 4 ml was selected as optimum. Results revealed that glutaraldehyde at 4ml concentration yielding microspheres having highest entrapment efficiency, capable to release drug for longer period of time.

Characterization of drug, polymer by Fourier Transform Infrared Spectroscopy

The FTIR spectral analysis of Nicorandil shows characteristics peak at 3218.17cm-1 due to N-H stretching. 2837.09, 2883.38, 2954.74cm-1 due to C-H group stretching, 1724.24cm-1 due to C=O stretching. Table No.2.

The physical mixture of drug and polymer were characterized by FTIR spectroscopy to investigate any physical as well as chemical interactions between the drug and polymer. The characteristic peaks of drug were retained in the physical mixture of drug and polymer. From the results it was confirmed that there is no interference in the functional group as the principle peaks of Nicorandil were found to be unaltered in drug polymer mixture. figure No.4,5

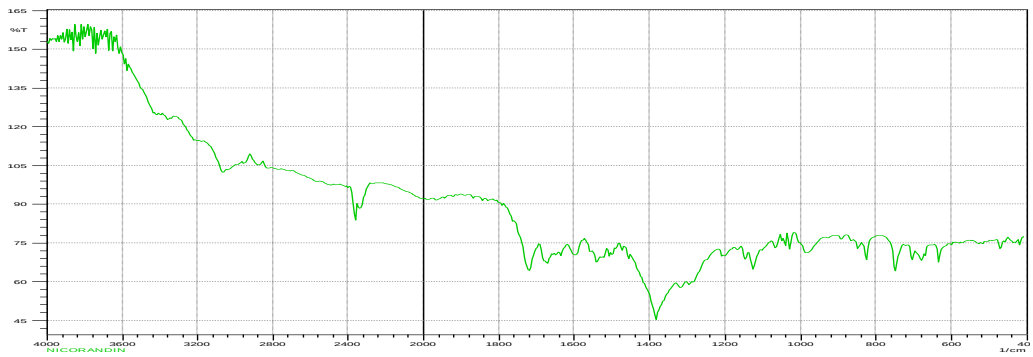

Figure No.4 : FTIR spectra of Nicorandil.

Table no. 2: Interpretation of FTIR spectra of Nicorandil.

Sr.no.	Characteristic peak (Wavenumber cm^{-1})	Group responsible
1	3218.17	N-H stretching
2	2837.09, 2883.38, 2954.74	C-H stretching
3	1724.24	C=O stretching
4	1473.51	C-H bending
5	1593.09	N-H bending
6	1296.86	O-NO_2 Stretching
7	1066.56	C-O stretching
8	1672.17	CO-NH stretching

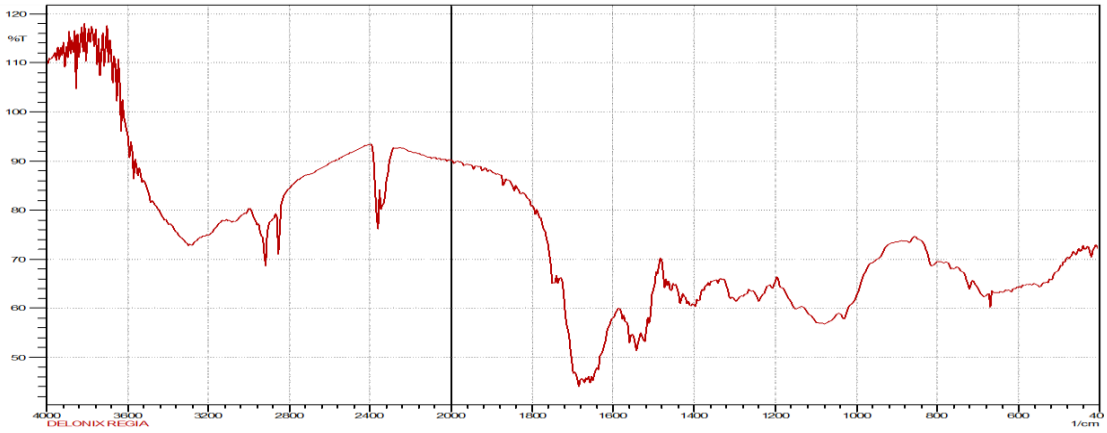

Figure No.5: FTIR spectra of Delonix Regia Gum.

Table no.3: Interpretation of FTIR spectra of Delonix regia gum.

Sr.no.	Characteristic peak (wavenumber cm^{-1})	Group responsible
1	3274.90, 3259.47, 3232.47, 3217.04	N-H stretch
2	2848.67, 2916.17	C-H stretch
3	1747.39	C=O stretch
4	1637.45	-C=C- stretch
5	3197.76	O-H stretch

EVALUATION OF SEMI-IPN MICROSPHERS

1. Drug Content and Entrapment Efficiency

The drug content of formulation F1-F9 prepared using different concentration of polymers was found to be in the range of (24.88 ±0.04) to (35.77±0.01). Percent entrapment efficiency of formulation F1-F9 using different concentration of polymers was found to be in the range of (49.77±74.57±0.05). The drug content and entrapment efficiency were found to be maximum for batch F5 i.e. 37.28±0.07 and 87.0 % respectively. (Refer Table No.4)

Table No.4: Drug content and % Entrapment Efficiency of Microspheres.

Batches	Drug Content (mg)	Entrapment Efficiency (%)
F1	24.88± 0.04	49.77±0.09
F2	29.05± 0.2	58.11±.0.08
F3	25.71±0.05	51.42±0.1
F4	34.42±0.04	68.85±0.08
F5	37.28±0.07	87.0±0.07
F6	30.80±0.08	73.6±0.03
F7	32.22±0.02	64.45±0.04
F8	34.85±0.03	69.71±0.06
F9	35.77±0.01	74.57±0.05

Each value represent mean ± standard deviation (n=3)

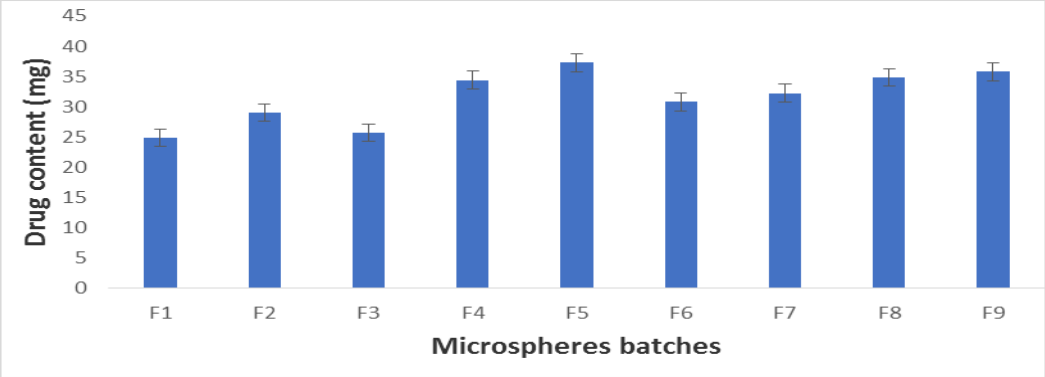

Figure No. 6: Drug content of microspheres.

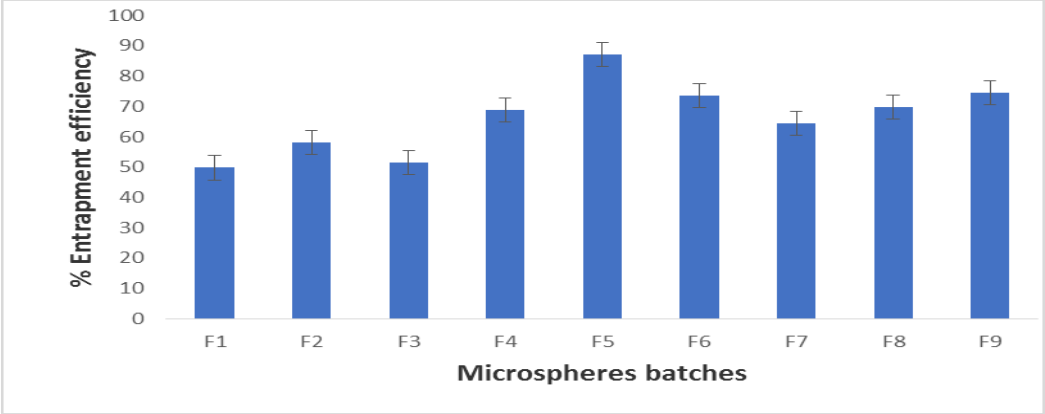

Figure No.7: % Entrapment Efficiency of microspheres.

2. Particle Size Analysis

The particle size of semi-IPN microspheres was found in the range of 109.22µm to 219µm. Results are shown in Table No.05 and Figure No.08,09 From the results it can be depicted that particle size of obtained microspheres shows dependence on nature, viscosity of polymeric solution and concentration of polymer. The particle size was found to be higher for batch F2 (121.61µm) than batch F1 (109.22µm), batch F5 (231.35µm) than batch F4 (153.47µm), batch F6 (206.2µm) than batch F7 (183.67µm). As the amount of neutral polymer increases, viscosity of polymeric solution also increases hence particle size was found to be increase.

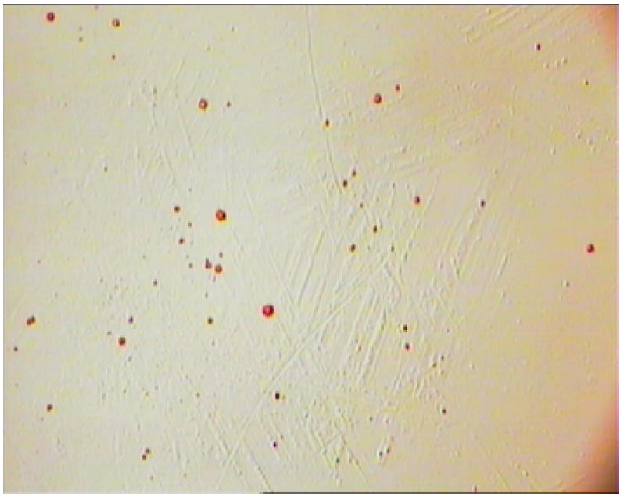

Figure No.8: Photomicrograph of microspheres.

Table No.5: Mean Particle size analysis of batches F1-F9.

Batches	Mean particle size (µm)
F1	109.22±0.68
F2	121.61±0.95
F3	90.96±0.74
F4	153.47±0.85
F5	231.35±0.62
F6	206.2±0.49
F7	183.67±0.54
F8	216.01±0.64
F9	219.01±0.42

Each value represent mean ± standard deviation (n=3)

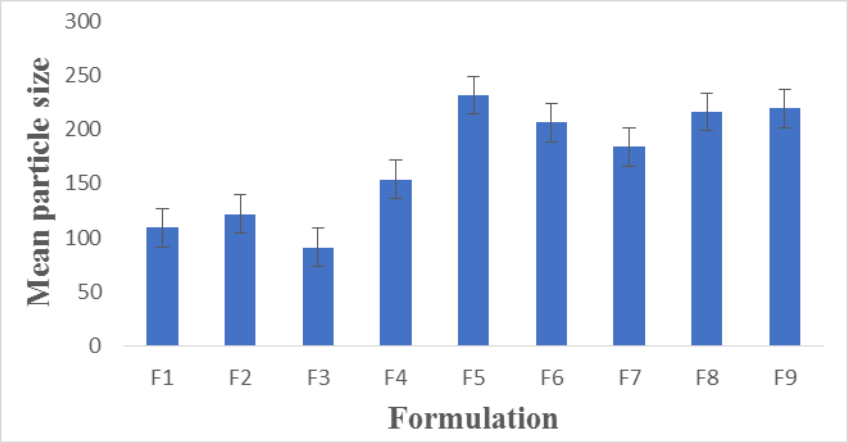

Figure No. 9 Mean particle size of microspheres batch F1-F9.

3. Swelling study

From the results it can be stated that the microspheres prepared from DRG as a neutral material showed higher swelling this may be due to hydrophilic nature of DRG. The batch F5 showed higher % swelling in pH 1.2 Acid Buffer and pH 6.8 phosphate buffer and it was found 65% and 125% respectively. Results are shown in Table No.6 and Figure No.10

Table No 6.: Percent water uptake of microspheres.

Batches	% Swelling study	
	pH 1.2	pH 6.8
F1	25.0±0.15	50.0±0.35
F2	50.0±0.78	62.5±0.60
F3	20.0±0.92	75.0±0.45
F4	37.5±0.30	100.0±0.57
F5	65.0±0.36	125.0±0.59
F6	55.0±0.35	92.5±0.30
F7	60.0±0.45	112.5±0.14
F8	42.5±0.40	87.5±0.60
F9	40.0±0.26	105.0±0.89

Each value represent mean ± standard deviation (n=3)

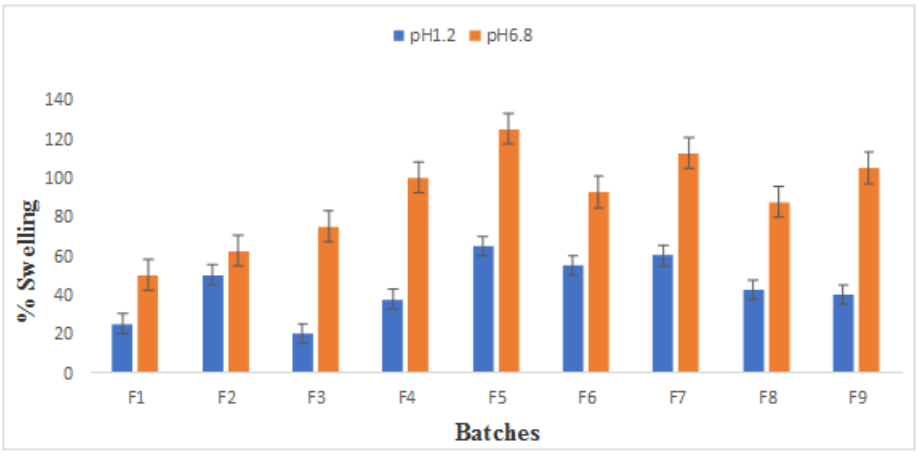

Figure No.10: Percent water uptake of microspheres batch F1-F9.

4. In vitro dissolution study

The release of Nicorandil was studied in pH 1.2 acid buffer and pH 6.8 phosphate buffer. The drug release from microspheres were found to be 71.13%, 41.60%, 70.75% for batches F1-F3 respectively. For batch F4-F6 (79.91%, 94.55%, 62.71%) and batch F7-F9 (53.05%, 75.59%). From the results, it can be observed that batch F5 has achieved 94.55% cumulative drug release. Effect of volume of glutaraldehyde: microspheres prepared by using 4ml of glutaraldehyde releases the drug slowly compared to the microspheres in which 2ml of glutaraldehyde used. From the data found that the amount of GA had a strong effect on in-vitro drug release. As the volume GA increased the drug release

decreased. Batch F5 shows higher drug release was found 94.55% upto 12 hrs respectively. Results are shown in Table No. 7, 8 and 9 and Figure No. 11,12,13.

Table No. 7: Percent Cumulative Drug Release of Nicorandil from Batch F1 to F3.

pH	Time (hrs)	% cumulative drug release		
		F1	F2	F3
0	0	0	0	0
1.2	1	12.0±0.34	2.085±0.58	6.24±0.52
1.2	2	19.29±0.36	3.519±0.69	11.90±0.39
6.8	3	35.04±0.59	5.56±0.79	19.39±0.38
6.8	4	40.99±0.56	7.88±0.88	35.04±0.48
6.8	5	45.21±0.49	11.28±0.92	41.18±0.61
6.8	6	52.41±0.52	15.11±0.98	45.50±0.53
6.8	7	55.77±0.78	19.60±0.96	52.60±0.73
6.8	8	59.71±0.57	25.05±0.71	55.68±0.69
6.8	9	65.08±0.65	30.68±0.62	59.71±0.59
6.8	10	68.54±0.71	35.92±0.82	64.89±0.68
6.8	11	71.13±0.71	41.60±0.74	68.25±0.78
6.8	12	-	-	70.75±0.82

Each value represent the mean ± standard deviation (n=3)

Table No. 8: Percent cumulative drug release of Nicorandil from batch F4-F6.

pH	Time (hrs)	% cumulative drug release		
		F4	F5	F6
0	0	0	0	0
1.2	1	2.69±0.76	8.27±0.52	2.95±0.25
1.2	2	30.16±0.79	16.75±0.39	7.03±0.66
6.8	3	34.73±0.88	25.79±0.38	8.57±0.78
6.8	4	39.59±0.92	35.20±0.48	19.33±0.54
6.8	5	44.67±0.98	45.08±0.44	26.43±0.92
6.8	6	50.13±0.96	55.21±0.50	29.60±0.57
6.8	7	55.57±0.79	60.43±0.60	33.32±0.64
6.8	8	60.76±0.81	67.00±0.71	37.82±0.73
6.8	9	64.28±0.98	73.98±0.76	42.96±0.86
6.8	10	68.42±0.97	84.55±0.81	48.86±0.78
6.8	11	73.91±0.94	87.55±0.85	55.33±0.87
6.8	12	79.91±0.62	94.55±0.39	62.71±0.42

Each value represent the mean ± standard deviation (n=3)

Table No.9: Percent cumulative drug release of Nicorandil from batch F7-F9.

pH	Time (hrs)	% cumulative drug release		
		F7	F8	F9
0	0	0	0	0
1.2	1	1.53±0.66	2.51±0.52	2.48±0.61
1.2	2	3.16±0.71	6.39±0.91	5.41±0.85
6.8	3	3.63±0.81	11.77±0.59	9.92±0.66
6.8	4	8.53±0.69	18.56±0.99	15.82±0.69
6.8	5	14.17±0.52	26.61±0.89	21.40±0.75
6.8	6	20.10±0.92	38.10±0.61	27.08±0.91
6.8	7	26.15±0.67	46.65±0.79	33.19±0.76
6.8	8	30.51±0.98	55.33±0.76	39.19±0.94
6.8	9	35.29±0.74	65.25±0.89	45.41±0.82
6.8	10	40.59±0.73	75.63±0.88	53.74±0.81
6.8	11	46.57±0.85	88.36±0.93	63.53±0.74
6.8	12	53.05±0.56	-	75.59±0.97

Each value represent the mean ± standard deviation (n=3)

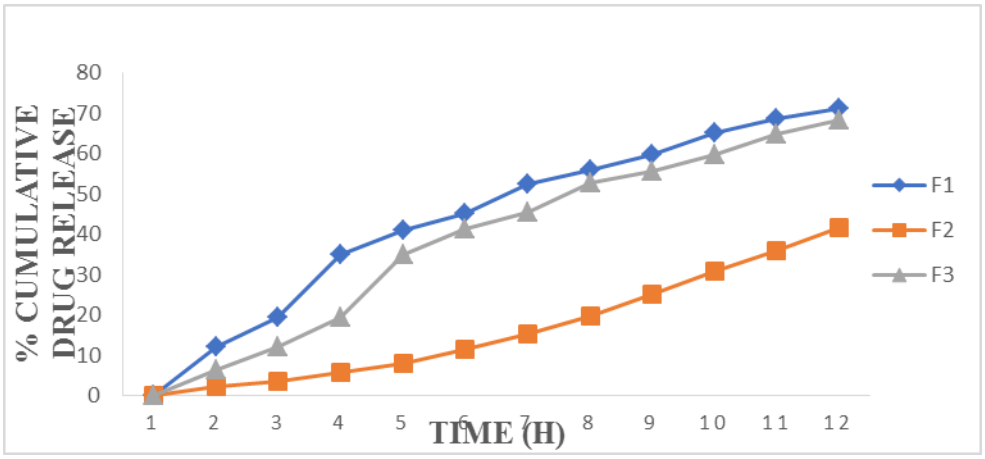

Figure No.11: In vitro drug release profile of Nicorandil batch F1-F3.

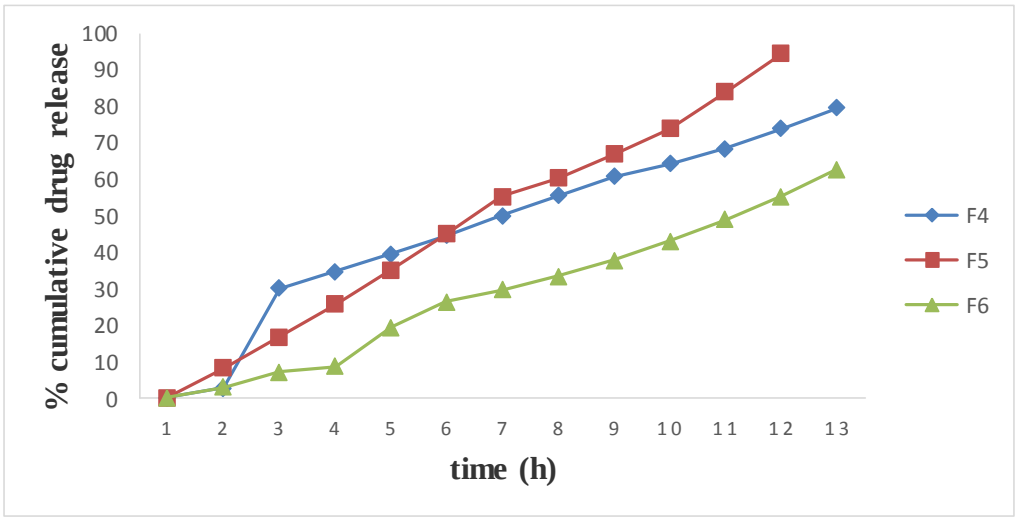

Figure No.12: In vitro drug release profile of Nicorandil batch F4-F6.

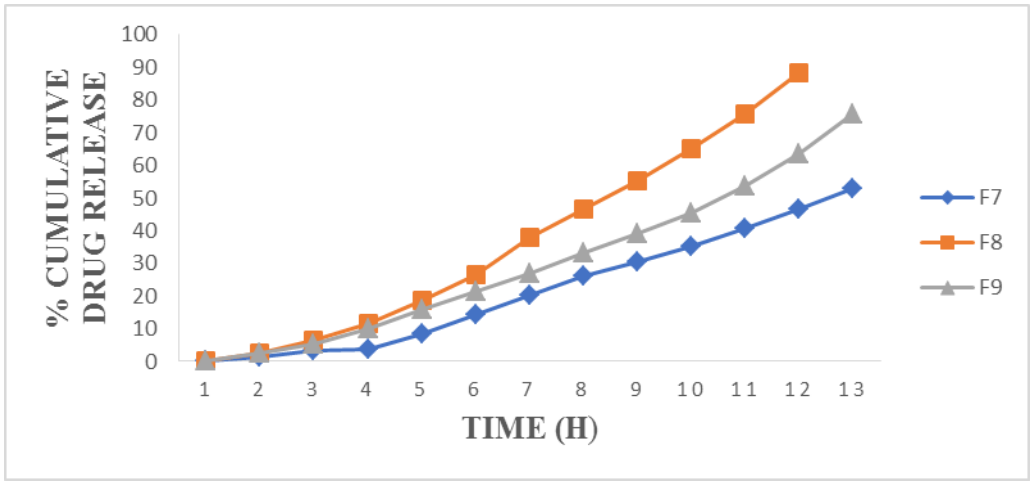

Figure No.13: In vitro drug release profile of Nicorandil batch F7-F9.

5. Characterization of optimized batch F5

1. FTIR Study of Optimized formulation

The FTIR spectral analysis of Nicorandil shows characteristics peak at 3218.17cm-1 due to N-H stretching. 2837.09, 2883.38, 2954.74cm-1 due to C-H group stretching, 1724.24cm-1 due to C=O stretching. Table No.10,11 the results it was confirmed that there is no interference in the functional group as the principle peaks of Nicorandil were found to be unaltered in drug polymer mixture. Figure No 14.

Table no.10: Interpretation of FTIR spectra of Nicorandil.

Sr.no.	Characteristic peak (Wavenumber cm^{-1})	Group responsible
1	3218.17	N-H stretching
2	2837.09, 2883.38, 2954.74	C-H stretching
3	1724.24	C=O stretching
4	1473.51	C-H bending
5	1593.09	N-H bending
6	1296.86	O-NO_2 Stretching
7	1066.56	C-O stretching
8	1672.17	CO-NH stretching

Table no.11: Interpretation of FTIR spectra of Delonix regia gum.

Sr.no.	Characteristic peak (wavenumber cm^{-1})	Group responsible
1	3274.90, 3259.47, 3232.47, 3217.04	N-H stretch
2	2848.67, 2916.17	C-H stretch
3	1747.39	C=O stretch
4	1637.45	-C=C- stretch
5	3197.76	O-H stretch

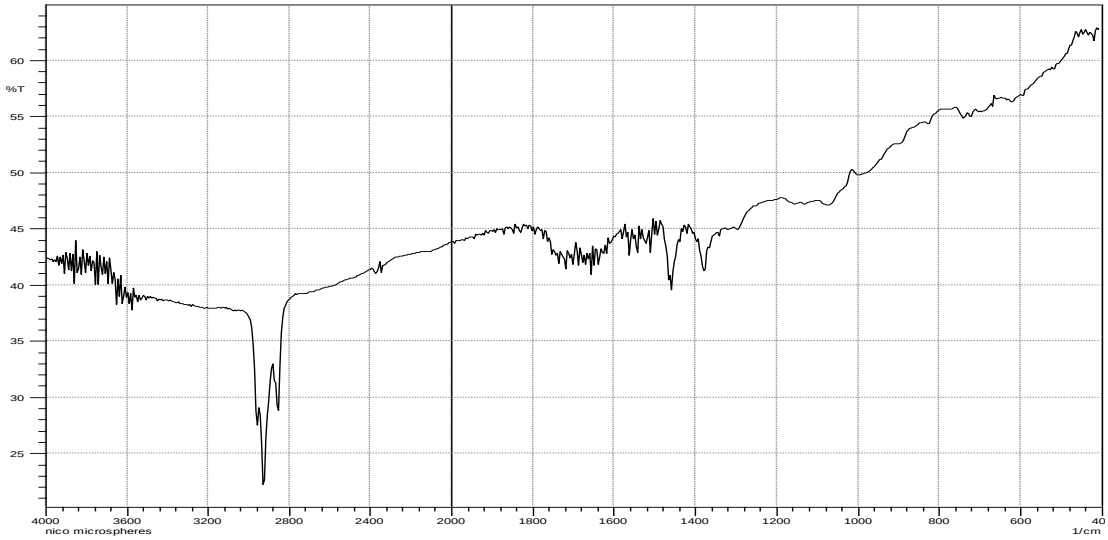

Figure No.14: FTIR spectrum of optimized formulation.

2. Scanning Electron Microscopy

From the SEM photography it was observed that formulated optimized microsphere (F5) was found to be spherical shaped without forming agglomeration and their surfaces are slightly rough. Results are shown in Figure No.15.

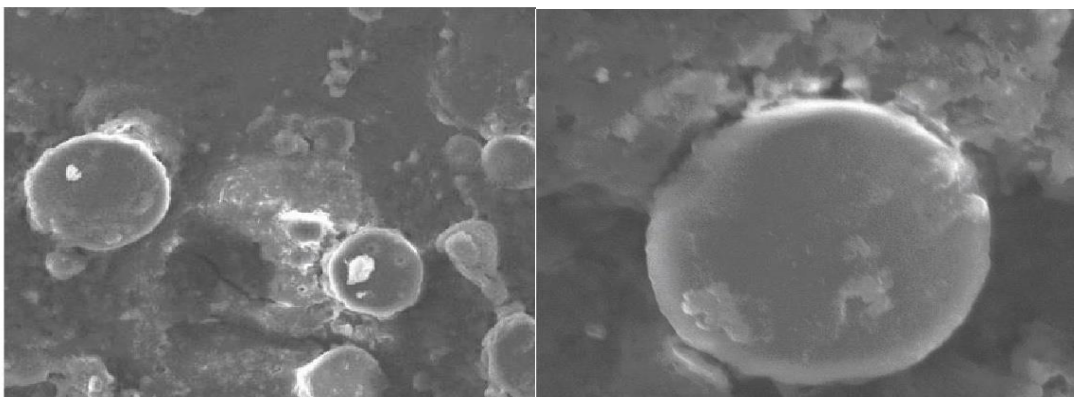

Figure No. 15: Scanning Electron Microscopy of optimized formulation (F5).

6.

7. Stability Study

Formulations showed good stability with no significant change in % drug loading, % EE and in in vitro drug release after stability study at 40oC ± 2oC and 75 % ± 5 % RH, for period of 3 months. Results are shown in Table No. 12,13 and Figure No.16. Hence prepared formulation was found to be stable.

Table No.12: Percent Drug Loading and Percent Entrapment Efficiency Study of Batch F5 Kept for Stability at 40± 2˚C/ 75± 5 % RH.

Temperature and %RH	Parameters evaluated	Duration			
		0 month	1 month	2 months	3 months
40^0C ± 2^0C 75 % ± 5 % RH	Drug content (mg/100mg of microns)	37.28±0.35	37.12± 0.15	37.09 ± 0.23	36.89± 0.34
	% Entrapment Efficiency	87.0± 0.43	87.02 ± 0.21	86.87± 0.13	86.75± 0.18

Each value represent the mean ± standard deviation (n=3)

Table No. 13: Percent Cumulative Drug Release of Nicorandil from optimized formulation (Batch F5) under stability study.

Time (Hr)	Percent Cumulative Drug Release*			
	0 month	1 month	2 months	3 months
0	0	0	0	0
1	8.27±0.52	8.38±0.63	8.23±0.54	8.19±0.55
2	16.75±0.39	16.66±0.36	16.54±0.51	16.52±0.37
3	25.79±0.38	25.75±0.54	25.64±0.56	25.22±0.51
4	35.20±0.48	35.30±0.27	35.45±0.24	35.47±0.76
5	45.08±0.44	44.07±0.45	44.18±0.39	44.15±0.22
6	55.21±0.50	55.19±0.57	55.48±0.33	55.38±0.16
7	60.43±0.60	60.45±0.72	60.59±0.41	60.49±0.45
8	67.00±0.71	67.83±0.65	66.58±0.74	66.45±0.37
9	73.98±0.76	73.95±0.48	73.85±0.63	73.75±0.59
10	84.11±0.81	83.25±0.55	83.17±0.35	83.12±0.73
11	87.55±0.85	87.43±0.73	87.49±0.31	87.39±0.36
12	94.55±0.39	93.43±0.79	93.35±0.29	93.25±0.27

Each value represent the mean ± standard deviation (n=3)

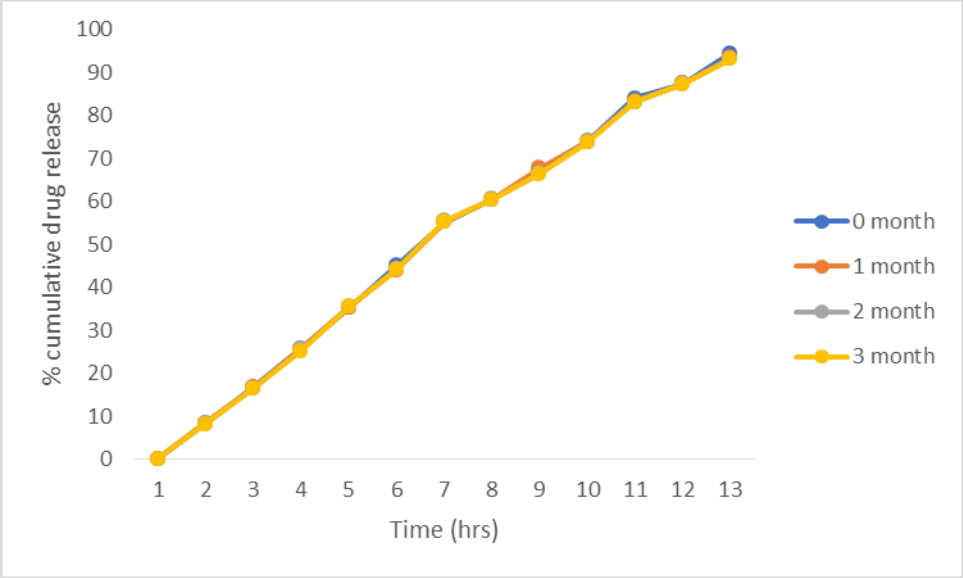

Figure No.16: In-vitro drug release study of Nicorandil from optimized batch (F5) Under stability study.

CONCLUSION

Continued release Nicorandil-containing semi-IPN microspheres were effectively created using the emulsion cross-linking technique and their drug release was investigated. The nature and various ratios of the polymers were discovered to be significant factors influencing the formulation's drug release pattern, swelling behavior, and entrapment efficiency.

Batch F5, which demonstrated 94.55% drug release over a 12-hour period, was optimal. This study examined the impact of cross-linker and polymer concentrations on medication release. Therefore, it can be said that the semi-IPN microspheres of nicorandil that were generated are capable of sustaining drug release and are beneficial to patient compliance due to their shortened dose interval. The natural and synthetic polymers used to construct the semi-IPN microspheres will help to overcome the drawbacks of the individual polymer network. The semi-IPN microspheres present novel opportunities and may find application as a drug carrier, contingent on the degree of drug loading and drug release.

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