PSYLLIUM-*G*-ALGINATE IPN BASED NANOPARTICLE DRUG CARRIER: FABRICATION, CHARACTERIZATION, AND OPTIMIZATION

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Abstract

By microwave irradiation, an interpenetrating polymeric network of the diabetes medication Metformin was created using a mix of the biopolymers Psyllium and sodium alginate. The reverse emulsion approach was used successfully to synthesize a metformin Psy-g-Alg nanoparticle. Box-Behnken design was used for the optimization of 3^3 levels to explore the effects of the independent variables Psy-g-Alg, Span 80, and Speed at three levels (-1, 0 and +1) on the output of the dependent variables particle size and% drug release at 8 h. The optimized Met-IPN-RE formulation was tested for particle size, in vitro drug release, swelling analysis, and XRD. All the research done indicate that this method is safe and effective for the oral delivery of antidiabetic medicines, despite its short elimination half-life and increased bioavailability.

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Introduction

Modern delivery studies' fundamental criteria are the creation of drug delivery systems for already-marketed pharmaceuticals for enhanced therapeutic indices and diminished toxicity features. This aids in enhancing the biodistribution and pharmacokinetics of medications for increased efficacy and effectiveness.[1] Researchers have recently focused extensively on the development of nanoparticle-based therapies due to its potential for site-specific action. In the drug delivery system, commercially accessible polymers play crucial functions, particularly in the nanocarrier system. Size and the ability to spatially and temporally manipulate distribution of drug have made nanoparticulate carriers appealing for quite some time.[2] Drug delivery systems are often prepared using polymers of natural origin, synthetic polymer, or interpenetrating polymer network (IPN), which are then transformed into nanoparticles for use as drug carriers. IPN are often produced by combining two or more polymers that have been synthesised and/or cross-linked in close proximity to one another.[3]–[5] IPNs are often made with natural polymers that have a viscous quality. Because of their naturally biodegradable composition, natural polymers can be safely ingested by mouth without risk of toxicity. Psyllium and alginate are two natural polymers often employed in drug delivery studies because they are excellent for IPN construction and allow for a sustained release of the drug.[6]

Psyllium is a natural ayurvedic plant and food-grade polysaccharide that has been widely utilized as a domestic cure from ancient times, across all cultures, against many ailments. Psyllium has the best potential to form a gel with water, making it a highly mucilaginous food-grade fibre. Psyllium mucilage has a molecular weight of around 1500 kDa and is made up of the structural units of arabinoxylan, which are made up of 22.6% arabinose, 74.6% xylose, and very small amounts of sugars. The medical and pharmacological uses of Psyllium mucilage are significant. Psyllium is used to treat a wide variety of digestive disorders, including indigestion, diarrhoea, diabetes, high cholesterol, atherosclerosis, ulcerative colitis, and cancer of the colon.[5], [7]

Alginate is produced by the cell walls of brown algae and other types of bacteria, and it belongs to the family of anionic natural polysaccharides. Alginate is a linear macromolecule made up of β-D-mannuronic acid (M) and α-L-guluronic acid (G) that are linked together at the 1-4 position. Nanoparticle, hydrogel may be formed with alginate across a wide range of pH and temperatures, making it an important polysaccharide. It has several uses in biomedicine thanks to its biodegradability, biocompatibility, and other biomedical-friendly properties. It has been shown experimentally that alginate can reduce blood glucose levels.[8]–[10]

The primary goals of the current investigation are to create Psyllium-g-Alginate (Psy-g-Alg) nanoparticles drug delivery system and to characterize and optimize their performance. Nanoparticles are optimized for sustained release characteristics by using metformin as a model medication and Psy-g-Alg IPN as the fabrication method.

Materials and Methods

Material

Sodium alginate, Genipin was procured from Sigma Aldrich, Mumbai, Psyllium purchesed from Bioprex Labs, Pune. Metformin received as gift sample from Lupin Limited, Pune. All other chemical with analytical grade was procured from Shreya chemical, Pune.

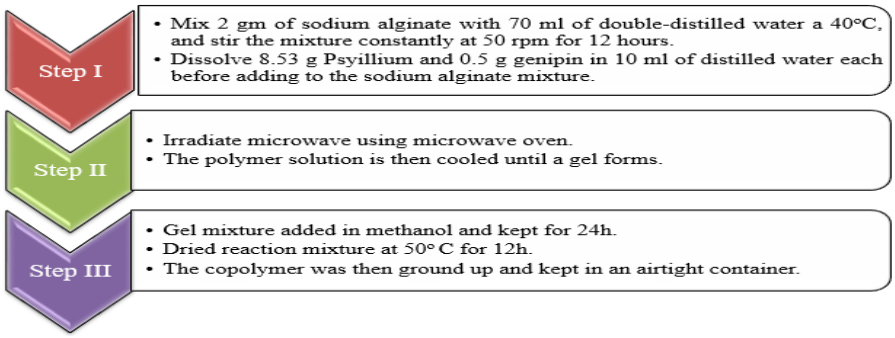
Methodology

Synthesis of Psyllium containing IPN resin system[9]

Graft copolymer grafting efficiency was calculated using the following formula:

% Grafting Efficiency = (W1- W0)/W2 x 100

where, W1 = weight of grafted copolymer; W0 = weight of native polymer;
W2 = weight of Psyllium.



Characterization of Synthesized (Psy-g-alg) IPN

FT-IR spectroscopy

The potential for an interaction between metformin and polymers was investigated by FTIR spectroscopy. Psyllium, and alginate each had their own FTIR spectrum obtained in this experiment. After combining 5 mg of chemicals with 200 mg of KBr, the mixture was pelletized at 1,000 psi. Finally, an FTIR Spectrometer (Model FTIR-8400s, Shimadzu, Japan) was used to acquire and evaluate FTIR data in the transmission mode over the range of 400 to 4000 cm^{-1}.[11]

DSC analysis

The medication, the IPN system, and the drug-loaded nanoparticles all underwent DSC testing. The samples were heated in a nitrogen environment (flow rate, 20 ml/min) at a heating rate of 10 °C min^{-1} from the temperature 25 to 500 °C.[12]

Rheological characterization

At temperatures of 93 and 115°C (200 and 240°F), a rheometer (Paar-Physica, MCR 301) was used to characterise the Psy-g-Alg IPN's rheology.[13]

Swelling behaviour

In 6.8 pH PB, laser light diffractometry was used to assess the swelling properties of Psy-g-Alg IPN. The samples were permitted to expand for 24 hours to ensure full equilibration.[14] (SHIMADZU - SALD 7001)

$D = (D - D_0)/D_0 \times 100$

Where D (%) represents the relative variation in mean diameter of particles; D_0 represents the mean diameter of dry particles (measured in acetone); and D represents the mean diameter of particles after 24 hours of swelling in buffer solution.

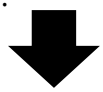
SEM analysis of Psy-g-Alg IPN

Microstructural examination of the samples was carried out using SEM on a Joel JSM-6380 LV type electron microscope. The voltage boost was 15 Kw.[15]

Preparation of Psy-g-Alg IPN Nanoparticles By Reverse Emulsion Method[16]

The pH of the solution was adjusted by dissolving 1% (w/v) Psy-g-Alg copolymer in 50 ml of 2% (v/v) acetic acid solution. The polymers solution was mixed with Tween 80 at 7400 rpm in an UltraTurrax homogenizer, and the resulting combination was dropped by the drop into 200 ml of Span 80-containing tone to create a W/O emulsion.

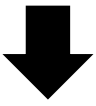
Testing was conducted using a Tween 80:Span 80 weight ratio of 1:4. Drop by drop, a 10% sodium sulphate solution was added to the emulsion while swirling for an additional 10 minutes, and the ionic crosslinking of polymers could be seen happening practically immediately.



The emulsion was transferred swiftly into a glass reactor where it was mechanically stirred between 1000 and 1700 rpm.

Using a decantation funnel, we combined equal parts glutaraldehyde and toluene to create glutaraldehyde-saturated toluene. The mixture was left to settle after being stirred for 10 minutes.

After separating the glutaraldehyde-saturated upper toluene layer, 20 mL of the solution was added to the W/O emulsion. A further 60 minutes were allotted for the mass to swirl in the reaction. The nanoparticles were finally isolated after 30 minutes of centrifugation at 20,000 rpm to separate the oil phase.



Multiple rinses of distilled water were used to remove the debris. Drying the resulting nanoparticles at room temperature followed.

Formulation code	% Psyllium-g-alginate	% Span 80	Speed (rpm)
REF1	0.5	0.1	1000
REF2	1.0	0.1	1000
REF3	0.5	0.2	1000
REF4	0.5	0.2	1500

Table 1: Preliminary trials for selection of working concentration range of the independent variables

Evaluation of drug loaded nanoparticles by reverse emulsion method (Met-IPN-RE)

Prepared metformin drug loaded IPN nanoparticles prepared by reverse emulsion method were determined for particle size, drug content, and *in-vitro* drug release.

Drug Content or metformin loading in nanoparticles (Met-IPN-RE)

A sonication bath was used to disperse 100 mg of nanoparticles in 10 mL of methanol (50 mg/mL) solution (1/1 v/v water and ethanol). After 24 hours of stirring, the suspension was settled using centrifugation (10,000 rpm for 15 minutes). The metformin nanoparticle loading was determined by measuring the drug concentration in the supernatant at 233 nm with a UV-VIS spectrophotometer (UV-1800, Shimadzu) in accordance with a standard calibration curve.[17]

Particle size analysis (Met-IPN-RE)

Dynamic light scattering (DLS) with a Malvern instrument was used to determine the drug nanoparticles' particle size distribution (mastersizer2000). Water or PB 6.8 pH was used as the measuring medium for nanoparticle size.[18]

***In-vitro* drug release studies (Met-IPN-RE)**

For in vitro release, 500 mg of metformin was loaded onto nanoparticles and suspended in 2 mL of buffer solution before being added to 100 mL of buffer solution in cellulose dialysis tubes kept at 37°C in a water bath with constant stirring. The concentration of metformin was measured by UV-vis spectroscopy in aliquots of buffer solution (5 ml) taken at certain times. Each experiment was done twice. The percentage of drug released after 8 hours was determined by dividing the total amount of drug put into the nanoparticle by the total amount of drug released.[19]

Optimization of The Experimental-Design For Nanoparticles

Box-Behnken analysis was used to analyse how various factors affected the formulation of metformin nanoparticles. To avoid aliasing of interaction variables and to conduct a thorough exploration of the design space, this architecture was opted upon. The nanoparticle formulation was refined using "Design-Expert® Software Version 9.0.4.1" ('Stat-Ease Inc., Minneapolis., USA.) by Abedullahh MH et al. Nanoparticle development variables that may have a major impact on drug release and particle size include surfactant concentration, grafted polymer concentration, and rotational speed (rpm). The components were coded as follows: A = % of Psy-g-Alg copolymer; B = % of Span 80; C = rpm; and the concentration of the factors was set at one of three levels (-1, 0 or +1, with 3 in center point). The dependent variables includes particle size and % drug release at 8 h. **Table 2** lists the individual variables, their ranges, and the limits that apply to them. In this example, out of the possible 3^3 experimental designs, 15 experimental runs are choosen **(Table 3).**[20]

Independent variables (i.e. Factors)	**'No. of Levels'**		
	Low (-1)	Medium (0)	High (+1)
A- % Psyllium-g-alginate	0.75	1.0	1.25
B- % Span	0.2	0.3	0.4
C- Speed	1500	1750	2000
Dependent Variables (Responses)	**Constraints (In range)**		
R1- Particle size	60-100 nm		
R2 - % drug release at 8 h	60-80 %		

Table:- 2 Different variables, levels and constraints in Box–Behnken Design for metformin nanoparticles by reverse evaporation method (Met-IPN-RE)

		Factor 1	**Factor 2**	**Factor 3**
Std.	**Run**	**A:Polymer conc.**	**B:Surfactant conc.**	**C:Speed**
		%	%	%
1	1	1	0.2	1750
13	2	1.5	0.3	1750
5	3	1	0.3	1500
7	4	1	0.3	2000
6	5	2	0.3	1500
3	6	1	0.4	1750
11	7	1.5	0.2	2000
15	8	1.5	0.3	1750
8	9	2	0.3	2000
2	10	2	0.2	1750

12	11	1.5	0.4	2000
14	12	1.5	0.3	1750
4	13	2	0.4	1750
10	14	1.5	0.4	1500
9	15	1.5	0.2	1500

Table:- 3 3^3 experimental design showing 15 runs

In vitro, drug release and the particle size of drug-loaded nanoparticles produced by the reverse emulsion method were investigated, and the optimized formulation was characterized for compatibility, particle size, zeta potential, XRD, and SEM studies.

Compatibility studies by FTIR for Met-IPN-RE nanoparticles

Nanoparticle formulation parameters, including particle size and in-vitro drug release, were assessed using FT-IR spectroscopy for structural features.

X-ray diffraction studies for Met-IPN-RE nanoparticles

The physical form of drug with nanoparticles was studied using X-Ray Diffraction. Nanoparticle diffraction patterns were obtained using Cu K 2α ray in a Brucker D 8 Advanced X-ray diffractometer at 40 kV and 25 mA of current.[21]

Surface morphology for Met-IPN-RE nanoparticles

A scanning electron microscope (Jeol, JSM-6360, Japan; 15 KV) was used to investigate the nanoparticles' topography. To examine the samples at 200-1000 nm, platinum films were sputtered onto them in a vacuum using a sputter coater (SPI SputterTM Coating Unit, SPI Supplies, Division of Structure Probe, Inc., PA, USA).[19]

Result and Discussion Preformulation Studies

Studies on drug-excipient compatibility

The results of the FT-IR analysis of Metformin HCl, sodium alginate, psyllium, and the admixture showed that the principal peaks of pure metformin appeared in all of the samples (Fig. 1). Based on FTIR analysis, we know that metformin HCl has a signature band at 1623 cm^{-1} associated with C=N stretching, another signature band at 1560 cm^{-1} associated with C=C stretching, two signature bands at 3369 and 3283 cm^{-1} associated with N-H primary stretching vibration, and a band at 3170 cm^{-1} associated with N-H secondary stretching.

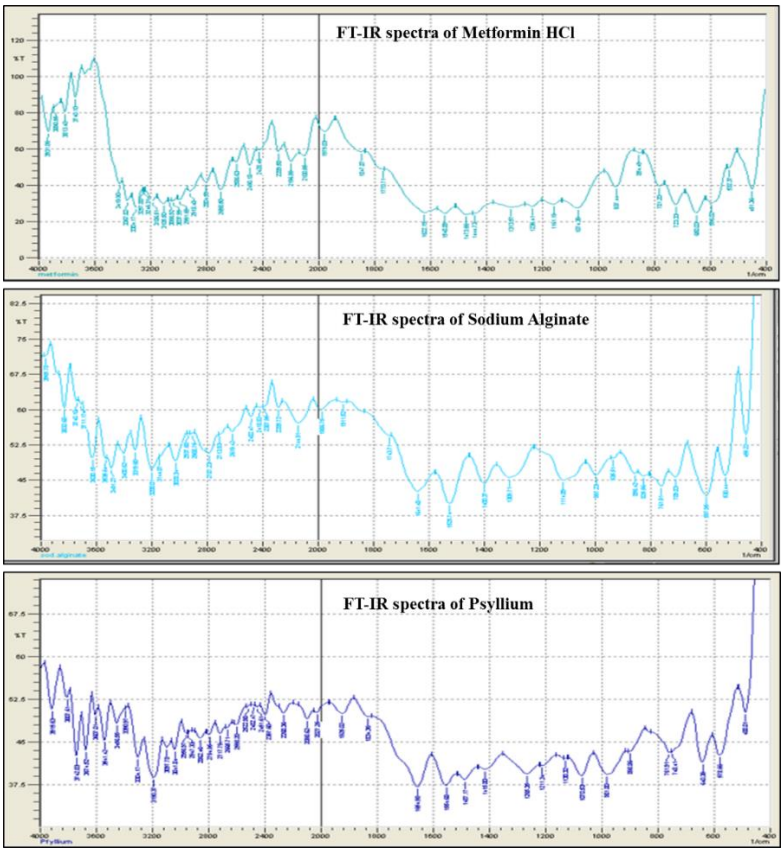


Figure:- 1 FT-IR spectra of pure metformin HCl, sodium alginate and psyllium

Results For Psy-g-Alg IPN

Psyllium containing IPN resin system is prepared with sodium alginate using genipin as crosslinker and further characterized.

Characterization of synthesized Psy-g-Alg. IPN

Studies on drug-excipient compatibility of Psy-g-Alg. IPN

These peaks are prominently appeared in admixture as well. Based on these findings, it appears that the IPN system does not interact with excipients.

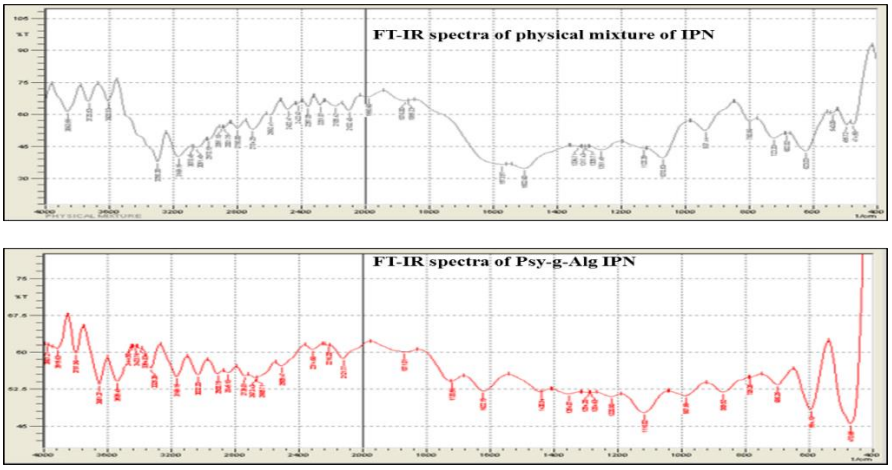


Figure:- 2 FT‑ IR spectra of Psy-g-Alg IPN and its physical mixture

DSC analysis for Psy-g-Alg. IPN

Figure 3 displays the IPN system's DSC thermogram. The drug's melting point, as depicted on the thermogram, occurred between 245 and 247ºC, after an initially flat profile. Drug and polymer mixtures similarly displayed a sharp drug peak that did not shift in position, indicating no drug-polymer interaction.

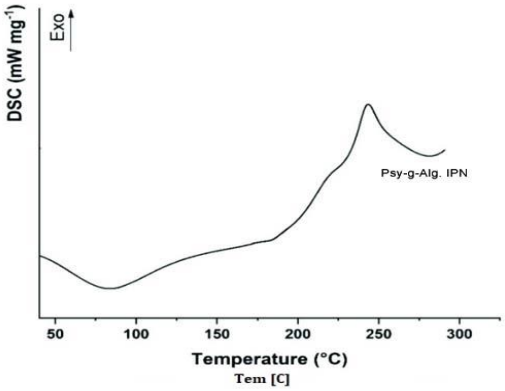


Figure:- 3 DSC thermogram of Psy-g-Alg IPN

Rheological characterization for Psy-g-Alg IPN

The rheological characteristics of the Psy-g-Alg. IPN was shown in **Fig. 4** As shear force and temperature increases the viscosity is reduced.

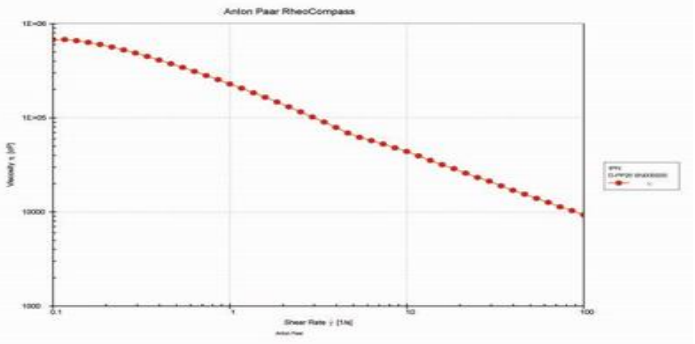


Figure:- 4 Rheogram of Psy-g-Alg IPN

Swelling behaviour of Psy-g-Alg IPN

The swelling characteristics of the Psy-g-Alg. IPN was shown in **Fig. 5.** As concentration of Psyllium and sodium alginate increases, the swelling behaviour also increased with time. Based on the swelling study as concentration of polymer increases, swelling of IPN increased.

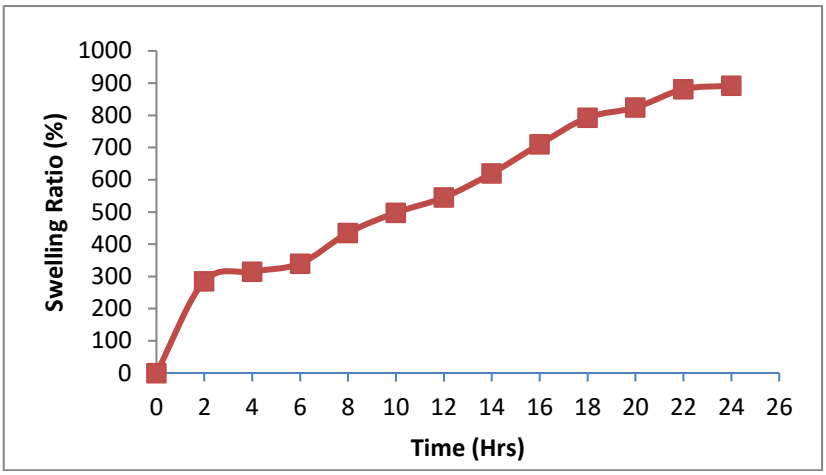


Figure:-5 Swelling study of Psy-g-Alg IPN

SEM analysis of Psy-g-Alg IPN

SEM image of the Psy-g-Alg. IPN was shown in **Fig. 6** The IPN system of Psy-g-Alg. Shows as networking structure.

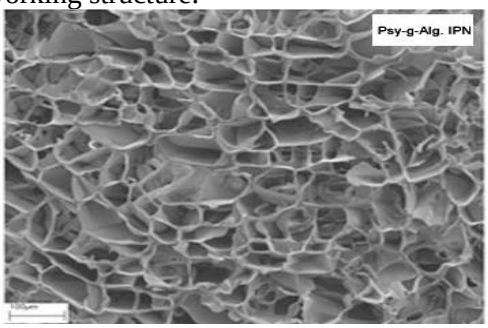


Figure:- 6 SEM Image of Psy-g-Alg IPN

Psy-g-Alg. IPN system is changing its physico-chemical characteristics. As concentration of Psyllium and sodium alginate increases the networking system is increasing and which leads to increase in viscosity of formulation.

As increase in temperature viscosity is reducing but the formation of IPN system is excellent complex formation, which helps in sustained release of drug from the IPN system.

Metformin Psyllium-g-Alginate (Met-IPN) IPN Nanoparticles Preparation By Reverse Emulsion Method (Met-IPN-RE)

Psy-g-Alg IPN nanoparticles prepared by reverse emulsion method and further evaluated.

Evaluation of Met-IPN-RE Nanoparticles prepared by Reverse emulsion method

Drug concentration, particle size, and in-vitro drug release were measured in the prepared nanoparticles. The results were shown in **Table 4**

Table 4 Evaluation of IPN nanoparticles prepared by Reverse emulsion method

Code	Drug Content (%)	Particle size (nm)
REF1	85.2	19.6
REF2	90.5	98.5
REF3	83.4	96.3
REF4	82.5	99.1

From the **Table 4** it can be inferred that as the stirring speed was increased from 1000 rpm to 1500 rpm particle size decreased so the speed range chosen was 1200-1700 rpm.

4.4.1.1 *In-vitro* drug release (Met-IPN-RE)

Table 5 Drug release of preliminary trial formulations

Time (hrs)	REF1	REF2	REF3	REF4
1	20.4	24.1	18.3	19.3
2	24.2	30.5	26.5	25.7
3	30.5	37.6	35.2	33.8
4	37.7	45.3	42.2	44.5
5	50.5	55.7	49.5	51.3

6	56.8	60.3	54.5	56.2
7	78.8	65.7	60.2	61.8
8	89.5	70.9	64.6	70.2

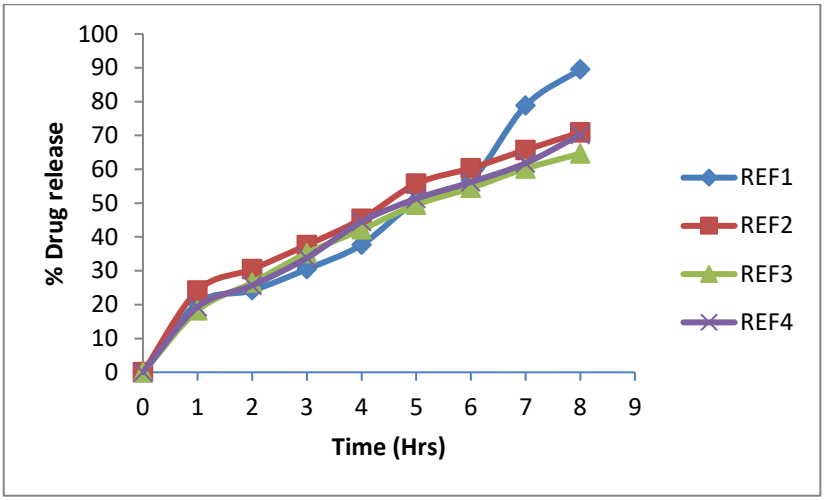


Figure:- 7 Drug release profile of trial formulations by reverse emulsion method

As the concentration of psyllium-g-alginate and Span 80 increased the drug release decreased so, the concentration range of psyllium-g-alginate was selected as 1.0-2.0% whereas, concentration range of Span was chosen as 0.2-0.4%.

Optimization of The Experimental Design For IPN Nanoparticles Prepared By Reverse Emulsion Method

The software used a Box-Behnken design, forecasting 15 iterations with 3 nodes. Particle size and percent drug release at 8 hours were used as dependent variables, and the optimal batch was determined by varying the values of the independent factors A: Psy-g-Alg, B: Span 80, and C: Speed (from -1, 0, +1). Table 6 displays batch-specific results.

Table 6 Design layout for Box-Behnken Run formulae

		Factor 1	Factor 2	Factor 3	Response 1	Response 2
Std	**Run**	**A:Polymer conc**	**B:Surfactant conc**	**C:Speed**	**Particle size (nm)**	**% Drug release in 8 hrs**
		%	%	%	nm	%
1	1	1 (-1)	0.2 (-1)	1750 (0)	99.5	85.5
13	2	1.5 (0)	0.3 (0)	1750 (0)	95.2	78.1
5	3	1 (-1)	0.3 (0)	1500(-1)	97.95	83.2
7	4	1(-1)	0.3 (0)	2000(1)	67.3	82.3
6	5	2(1)	0.3(0)	1500(-1)	95.8	72.2
3	6	1(-1)	0.4(1)	1750(0)	64.8	81.1
11	7	1.5(0)	0.2(-1)	2000(1)	84.2	80.6
15	8	1.5(0)	0.3(0)	1750 (0)	89.2	78.3
8	9	2(1)	0.3(0)	2000(1)	95.7	64.6
2	10	2(1)	0.2(-1)	1750(0)	94.8	62.7
12	11	1.5(0)	0.4(1)	2000(1)	71.5	60.3
14	12	1.5(0)	0.3(0)	1750(0)	90.8	78.6
4	13	2(1)	0.4(1)	1750(0)	89.6	53.97
10	14	1.5(0)	0.4(1)	1500(-1)	94.2	57.7
9	15	1.5(0)	0.2(-1)	1500(-1)	91.4	69.8

Evaluation of metformin loaded nanoparticles by reverse emulsion method (Met-IPN-RE)

Prepared metformin loaded nanoparticles prepared by reverse emulsion method were evaluated and optimized formulation was characterized for compatibility, particle size, zeta potential, XRD and SEM studies.

Particle size determination for Met-IPN-RE

Particle size is seen to increase as concentration of the psyllium-g-alginate IPN rises. As the concentration dropped, the particle size shrank. The particle size lies within 64.8 to 99.5 nm. Particle size reduced with increase in stirring speed. Results are showed in **Table 4**

In-vitro drug release for optimized formulation Met-IPN-RE

Metformin HCl IPN-Nanoparticles (Met-IPN-RE) were formulated to attain the sustained release of metformin HCl. The optimized batch of nanoparticles (Psy-g-Alg: 1.84 %w/v, Span 80: 0.306% w/v and Speed: 1978.05 rpm) showed 69.76% release of metformin HCl in 8 h **(Fig. 8).** The drug release profile of prepared Met-IPN-RE compared with marketed Glycomet 500mg SR tablet formulation. The results indicates that Met-IPN-RE (69.75%) better release profile than that of marketed Glycomet tablet (61.75%) as shown in figure 8)

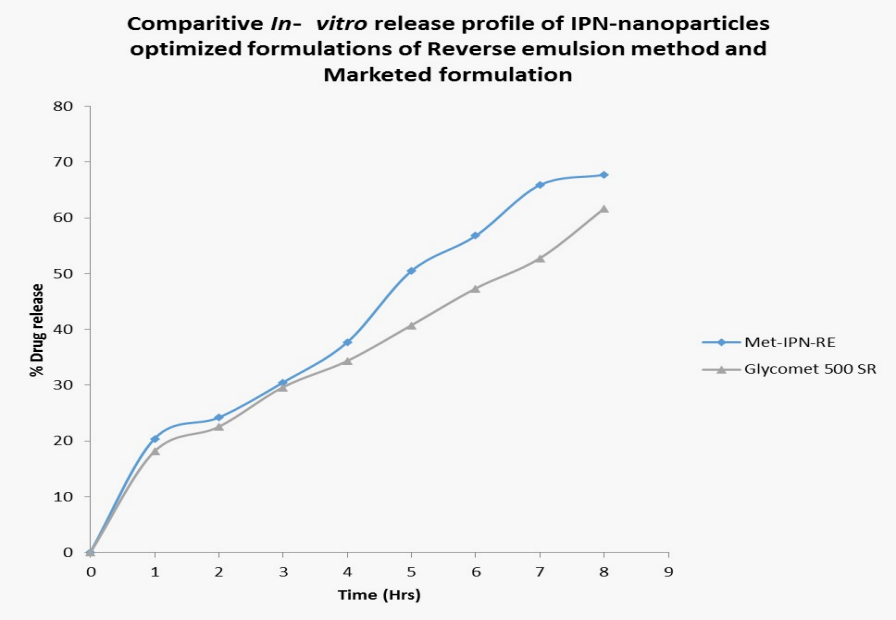


Figure:- 8 *In-vitro* release profile of IPN-nanoparticles optimized formulation reverse emulsion method and Marked formulation

The kinetics of drug release from the optimised batch were approximated using four different models: zero-order release, first-order release, Higuchi's, and Korsmeyer-Peppas'. For the optimised formulation, R^2 values of 0.9854, 0.9527, and 0.9441 were obtained from the zero-order model, the first-order model, and Higuchi's model, respectively. Drug release follows a non-fickian diffusion pattern linked to matrix release, as indicated by Korsemeyer-Peppas (n) = 0.64. Based on these findings, it appears that the optimised metformin HCl formulation has prolonged drug release.

Results of ANOVA of quadratic model of IPN nanoparticles prepared by Reverse emulsion technique

To determine how desirable each element was throughout all of the different batches of experiments, an ANOVA was performed, and a quadratic model was selected. The results showed that the applied model was appropriate, with both significant fit p-values and non-significant lack of fit p-values for R1 and R2 responses across all trials. The model's applicability is demonstrated by the high R2 values obtained for both the R1 and R2 responses. Table 7 displays the results of an analysis of the quadratic model using polynomial equations. Surface response plots **(Fig. 10)** and accompanying contour plots **(Fig. 9)** define the influence of various parameters on R1 and R2 based on the constraints specified in the model. Drug release after 8 hours (as a percentage) varied from 53.97 to 85.6%, while particle size was found to be between 64.8 and 99.5 nm. The drug release was suppressed by an increase in A and B concentrations. According to the findings, Variable C is the true culprit in the particle size distribution.

Table 7 Results of ANOVA of linear model for IPN nanoparticles prepared by reverse emulsion method

'Response	'Model	F-Value	p- Value (Prob > F)	R^2 - Value	Lack. of Fit	Lack. of Fit p- value
R1 (Release at 8 h %)	Linear	8.19	0.0038 significant	0.6908	0.39	0.0012
	Model equation (Coded): R1 = +72.60-9.83*A-5.69*B+0.6125*C					
R2 (Particle size, nm)	Linear	12.64	0.0007 significant	0.7752	0.13	0.0149
	Model equation (Coded): R2 = +128.80+19.29*A -22.73*B -45.08*C					

In light of these findings, the system was programmed to produce a solution with a desirability rating of 1 using the desirability plot depicted in Fig. 4.9. A (1.485% w/v), B (0.3963%w/v), and C (1843.6 rpm) were chosen according to their respective estimated particle sizes of 89.474 nm and 67.61% drug release at 8 h. In contrast, Table 7 shows that the experimental values for particle size are 91.78±1.71 (% error 2.39), and that the experimental values for drug release after 8 hours are 68.76±2.83 (% error 2.5). These numbers indicated that the optimised batch of experimental nanoparticles produced results that matched those expected by the algorithms. The experimental findings for optimised nanoparticles, including the magnitudes of the various parameters used, are shown in Table 8.

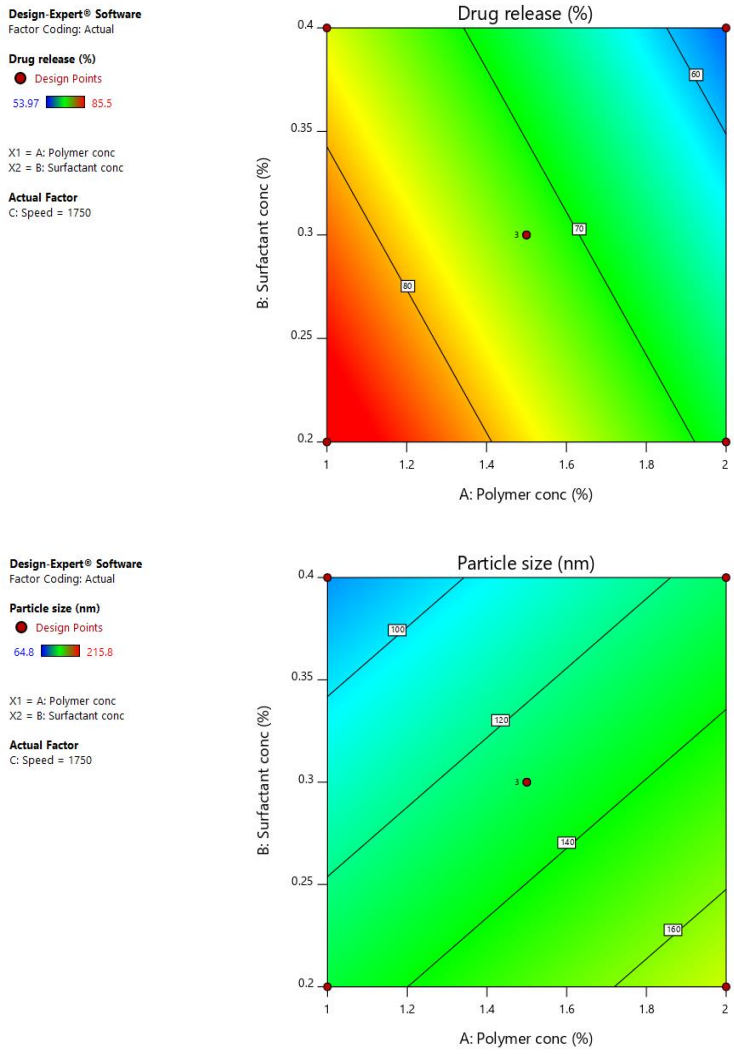
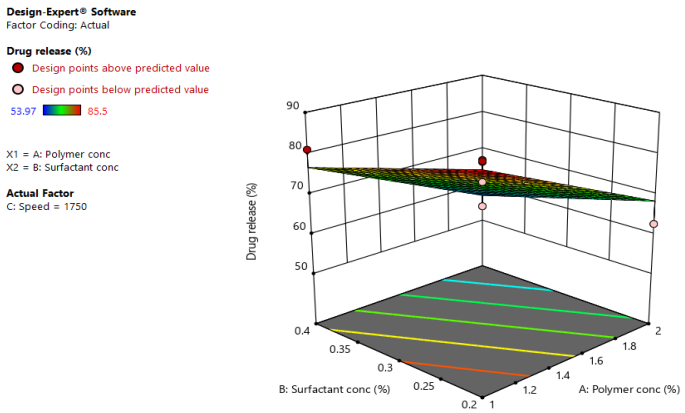


Figure 9: Contour plot for % drug release at 8 h and particle size.



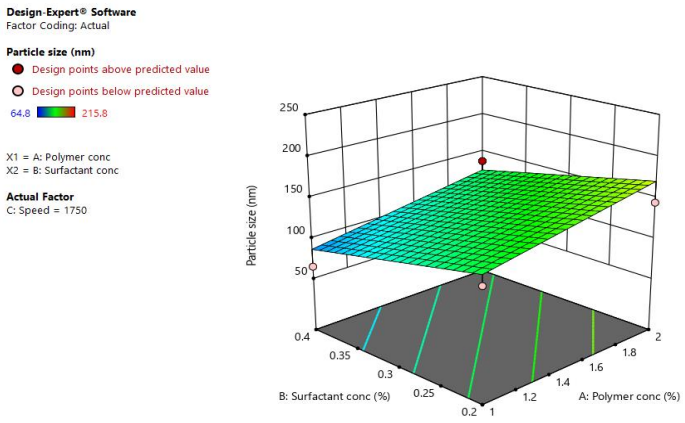


Figure:- 10. Response surface plot for % drug release at 8 h and particle size

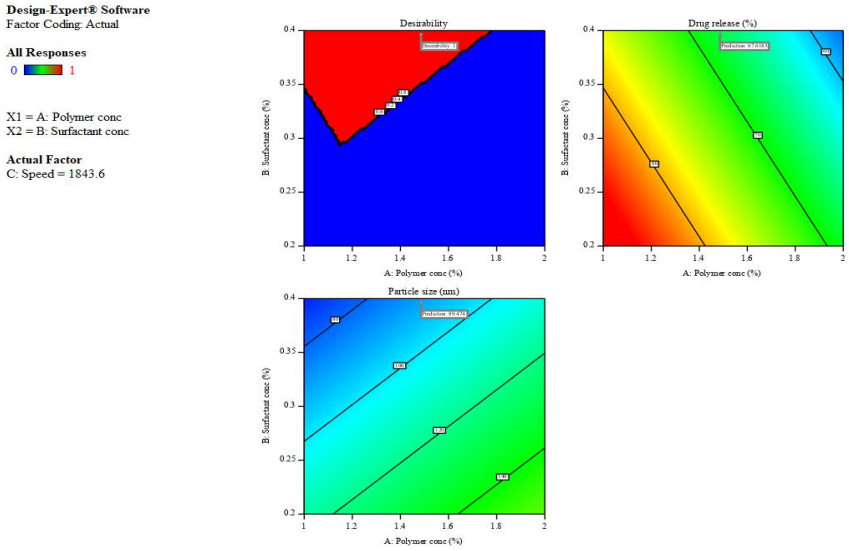


Figure:- 11 Desirability plot for the software generated formulation

Desirability value is 1 which validates the optimization model and process.

Table 8. Predicted. and observed values of responses for optimized batch of IPN nanoparticles

'Responses'	'Predicted - Value'	'Observed - Value'	%- Error*
% Release at 8 h	67.61±6.48	68.76±2.71	2.5
Particle size (nm)	89.474±2.8	91.78±3.83	2.39

***% -Error = ('observed value' – 'predicted value')/'predicted value' × 100**

Table 9. Optimize batch of IPN nanoparticles prepared by reverse emulsion method

A	B	C	R1 (nm)	R2 (%)	Desirability
1.485	0.3963	1843.6	91.78±3.8	68.76±2.71	1.0

Characterization of Optimized Nanoparticles Formulation Prepared By Reverse Emulsion Method

Prepared drug loaded nanoparticles prepared by reverse emulsion method were characterized for compatibility, particle size, zeta potential, XRD and SEM studies.

Compatibility of optimized IPN nanoparticles

Compatibility between drug and excipient in Psy-g-Alg IPN nanoparticles were found to be compatible and no such changes were observed.

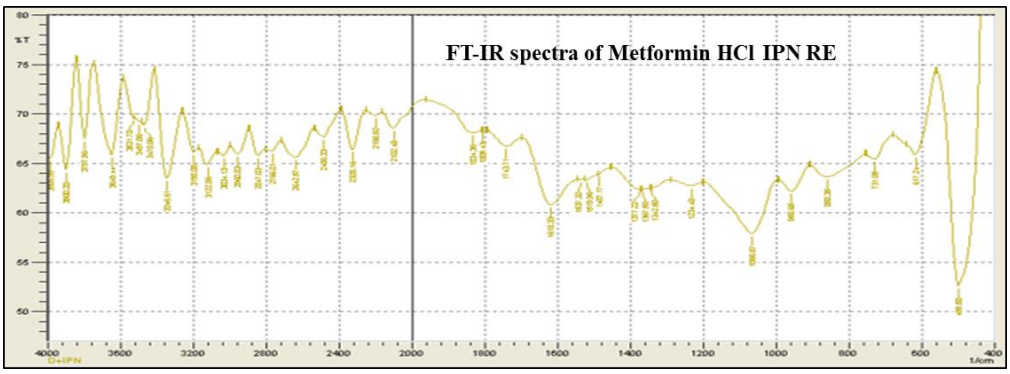


Figure:- 12 FTIR of optimized nanoparticles by reverse emulsion method

Particle size and zetapotential determination of optimized Met-IPN-RE nanoparticles

There is increase in particle‑size with increase in Psy-g-Alg concentration is observed. Particle size reduced with the decrease in concentration. The particle size lies within 63.5 to 99.6 nm. Particle size reduced with increase in stirring speed. Results are showed in **Figure 13**

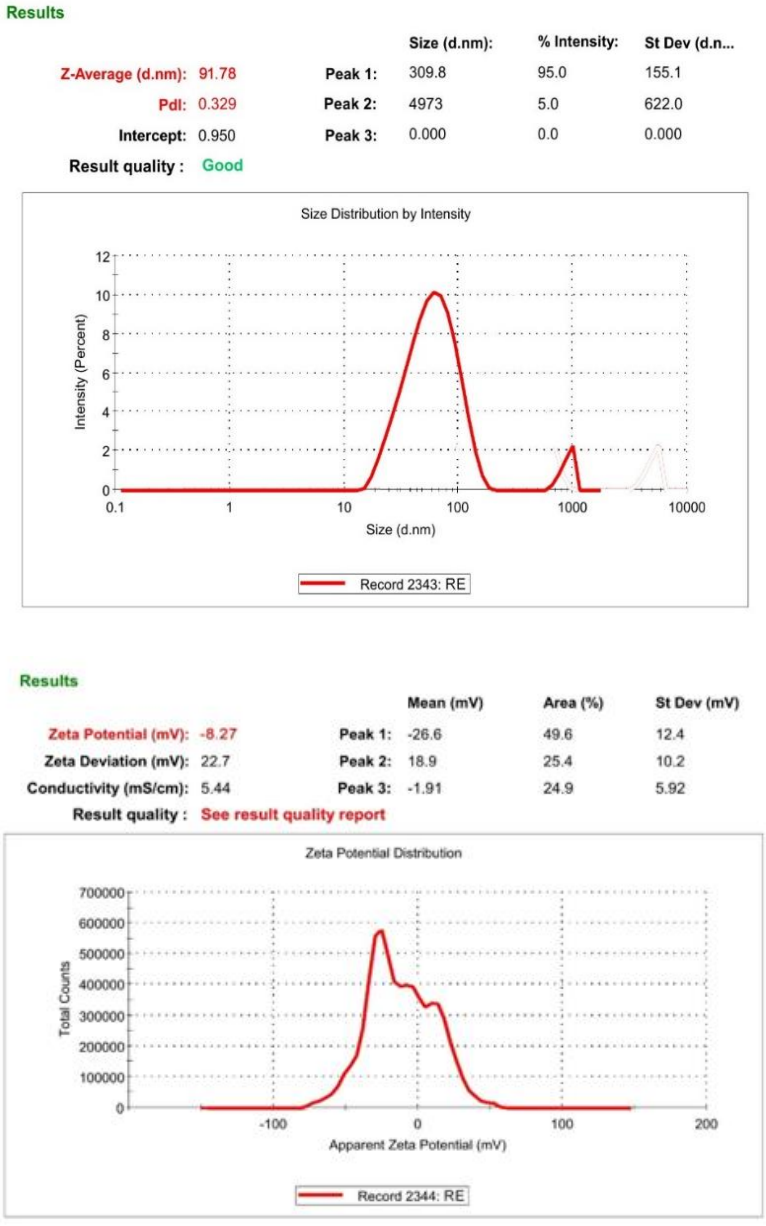


Figure:- 13 **Particle size and zetapotential of Met-IPN-RE NPs prepared by reverse emulsion method**

X-ray diffraction studies for Met-IPN-RE

The physical form of drug with nanoparticles was studied using X-Ray Diffraction. XRD studies revealed that the optimized Met-IPN-RE nanoparticles converted to amorphous, where pure metformin was crystalline in nature. **(Fig. 14).**

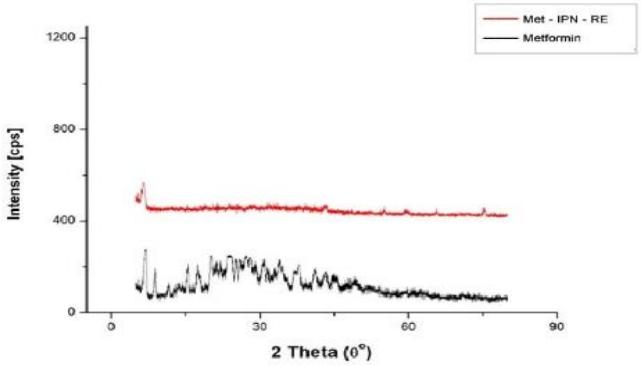


Figure:- 14 XRD of optimized Met-IPN-RE nanoparticles by reverse emulsion method

SEM of optimized IPN nanoparticles

The formation of poly dispersed nanoparticles, in accordance to literature data. SEM images revealed that the particles are 'spherical in shape' **(Fig. 15).**

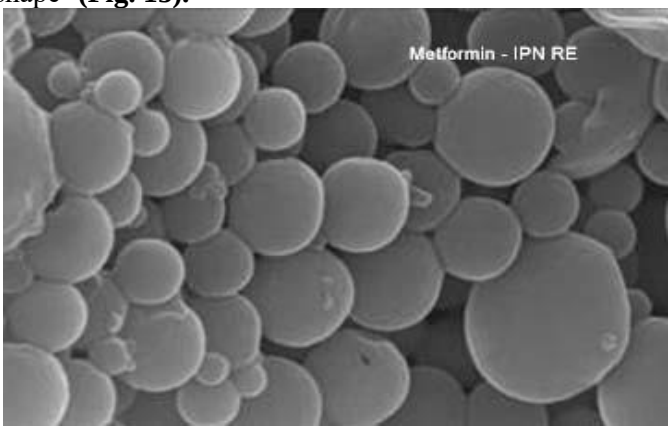


Figure:-15 SEM of optimized Met-IPN-RE nanoparticles by reverse emulsion method

Based on the results it can be concluded that IPN nanoparticles formulation prepared by reverse emulsion method was formulated in order to achieve the sustained delivery of metformin HCl can be achieved through unique nanoparticles system.

Conclusion

The natural polysaccharide psyllium and alginate containing IPN was successfully fabricated using genipin as crosslinker by using microwave irradiation method. Formulated Psy-g-Alg IPN characterised using FT-IR spectroscopy, DSC analysis, Rheological characteristic, Swelling behavior and SEM analysis. Formulated Psy-g-Alg IPN shows no internation with excipents, proper networking structure, improved selling beviour, and temparature dependent viscosity. Even though viscosity decreases with rising temperature, the IPN system forms a good complex that aids in the sustained release of the drug.

The reverse emulsion approach was used successfully to synthesise a metformin Psy-g-Alg nanoparticle. Box-Behnken analysis was used to formulate an improved Met-IPN-RE. The sustained drug release profile of the formulation is superior to that of currently available sustained release formulation. Anti-diabetic medications will be most effectively delivered over the long term if they are packaged in an IPN nanocarrier. Anti-diabetic medication pharmacological testing in humans and animals is anticipated to be more in-depth.

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