

“Synthesis of Water Swelling Polymer and Its Characterization for Development of Drug Delivery System”

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ABSTRACT: - The aim of present study is to synthesize water swelling polymer for the development of drug delivery system. An attempt will be made to prepare cross-linked polymethacrylic acid polymer by optimizing initiator, solvent and monomer :cross-linker concentration ratio to give comparatively more water absorption capacity. These polymers can be further used in the drug delivery system. 125g/g as compared to 0.025g (batch I1) , 0.05g(batch I2) and 0.1g(batch I4) with water swelling capacity of 75g/g, 110g/g and 90g/g respectively. At low concentration of initiator, few numbers of chains are initiated leading to the formation of longer polymer chain length and higher molecular weight polymer with high water swelling capacity. The concentration of initiator is inversely proportional to the molecular weight of polymer. Increasing the concentration of initiator, i.e. higher number of free radical initiates the larger number of small chains forming lower molecular weight polymer results in an increase in the water swelling capacity. At 0.1g of benzoyl peroxide, low water swelling capacity, and partial water solubility was observed because of very small particles of polymer with low cross-linking.

Chloroform solvent system was selected for the preparation of water swellable polymer (Batch S2) on the basis of maximum water swelling capacity with 125g/g and 91% of percentage yield as compared to toluene (Batch S1) and ether (Batch S3) with water swelling capacity of 88g/g and 95g/g respectively as shown in table 17. Where reaction were carried out at 111^oC, 80^oC and 61^oC for toluene ether and chloroform respectively under reflux.

Spectral analysis of prepared water swellable polymer showed the presence of C-O-C ether linkage at wave number 1106cm⁻¹ which implied monomer-cross linker linkage and CH₂ stretching at

wave number 3206cm⁻¹ implied that monomer-monomer linkage(Table No. 23) confirmed the structure of prepared water swellable polymer. Batch P11 having initiator concentration 0.075g, chloroform as a solvent and monomer: cross- linker ratio 9.0:1.0 was considered for the preparation of drug delivery system i.e. gel (Table 05).

I. INTRODUCTION:

A polymer (poly- "many" + -mer "parts") is a large molecule or macromolecule composed of many repeated subunits. The simplest definition of a polymer is something made of many units. Polymers both natural and synthetic are created via polymerization of many small molecules, known as monomers.^[1]

Polymers are used in industries and have the various applications, even the items like plastic bags, rubbers, pipes, bottles etc are made of polymers. Industrially polymers are used in packaging materials, building and constructions, electrical and electronics, agriculture and automotive etc.^[2]

Water absorbent polymers are the polymers which absorbs water and swells. e.g. crosslinked polyacrylic acid, starch, polyaspartic acid, polymeric derivative of acrylic acid and polysaccharides.^[10]

Superabsorbent polymers are the water absorbent polymers which absorb water more rapidly. According to “modern superabsorbent polymer technology” these polymers are non-systemic, non-toxic,non-digestive water absorbent polymers which absorbs water rapidly e.g.cross-linked polyacrylic acid.^[11]

II. MATERIAL AND METHODS:

The water swellable polymer can be used in the various fields such as industry, agriculture, food and medicine. The cross-linked polymers of

acrylic acid, starch, aspartic acid and naphthyl derivative of acrylic acid and saccharides etc were used for their water absorbent property for agricultural field to absorb water for crops, sanitary napkins, paper diapers, disposable dust cloth for kitchens, absorbent diapers, sludge coagulants, hygienic goods, dehydrating agents etc.

Acrylic Acid(Loba Chemicals, Mumbai.)
Methacrylic acid(Loba Chemicals, Mumbai.)
Benzoyl Peroxide(Loba Chemicals, Mumbai.)
Allyl Bromide(Loba Chemicals, Mumbai.)
Sucrose(Loba Chemicals, Mumbai.)
Diclofenac Sodium(ZimLab,Nagpur)
Chloroform(Loba Chemicals, Mumbai.)
VoveranEmugel(Novarties Pvt. Ltd.)

Method:

For the synthesis of allyl sucrose, sodium sucrose was synthesized by taking 11.4g of sucrose and 2.6g of NaOH in 1 ml water and this mixture was heated at 65°C for 1.5hr in the beaker. Then the blend was removed by addition of 10ml of chloroform. The removed dried solid material was triturated in mortar. The fine powder of sodium sucrose was kept into desiccators. Then this fine sodium sucrose was taken into a round bottom flask (250ml) with 10 ml of chloroform. 24.2 g of

allyl bromide was added drop-wise through dropping funnel in to the above prepared solution. This solution was continuously stirred for 3 hr under reflux at 67°C. After 3 hr preparation was removed and took into the separating funnel, 30 ml water was added, and shaken for 5 min. Chloroform layer was separated which contained sucrose acrylate. TLC was carried out for the detection of presence of any byproduct. There was single spot; product was confirmed to be pure.

Allyl sucrose Boiling point: - 70-72 °C

Appearance: - light yellow liquid **Solubility:** - Insoluble in water, soluble in chloroform, ether. %

Yield: - 93

General procedure of polymerization

1. Take 50 ml porogen in 4 necked RBF (N₂ purging for 1 hr at 65c)
2. Addition of initiator
3. Drop wise addition of mixture of monomer and cross- linker through dropping funnel(reflux condenser)
4. Continuously stirring for 4 hr.
5. Recovery of prepared polymers.
6. Dried and finally divided
7. Evaluation of water absorption capacity.

(Table no. 01) Optimization of initiator concentration

Formulation code	Monomer : Cross-linker (g:g)	Initiator (g)	Solvent (Porogen)
I1	8.0:2.0	0.025	Chloroform
I2	8.0:2.0	0.05	Chloroform
I3	8.0:2.0	0.075	Chloroform
I4	8.0:2.0	0.100	Chloroform

(Table no. 02) Water swelling capacity and %yield for the batches of different initiator concentrations

Formulation code	Initiator (g)	Water swelling capacity (g of water/1g of polymer)	% Yield
I1	0.025	75	83
I2	0.05	110	86
I3	0.075	125	91
I4	0.1	90	79

Procedure for synthesis of cross-linker^[71]

Procedure: For the synthesis of allyl sucrose, sodium sucrose was synthesized by taking 11.4g of sucrose and 2.6g of NaOH in 1 ml water and this mixture was heated at 65°C for 1.5hr in the beaker. Then the blend was removed by addition of 10ml of chloroform. The removed dried solid material was triturated in mortar. The fine powder of sodium sucrose was kept into desiccators. Then this fine sodium sucrose was taken into a round bottom

flask (250ml) with 10 ml of chloroform. 24.2 g of allyl bromide was added drop-wise through dropping funnel in to the above prepared solution. This solution was continuously stirred for 3 hr under reflux at 67°C. After 3 hr preparation was removed and took into the separating funnel, 30 ml water was added, and shaken for 5 min. Chloroform layer was separated which contained sucrose acrylate. TLC was carried out for the

detection of presence of any byproduct. There was single spot product was confirmed to be pure.

(Table no. 03) Physical characteristics of allyl sucrose

Product	Boiling point	Appearance	Solubility	% Yield
Allyl sucrose	70-72 °C	light yellow liquid	Insoluble in water, soluble in chloroform, ether.	93

TLC is carried out and a single spot is spotted. The product was confirmed to be pure.

powder was then placed in dye cavity of pellet machine and 10psi pressure was applied. The prepared potassium bromide pellet was kept in IR cell and results were recorded as shown in

IR spectral study

Procedure: About one drop of allyl sucrose was taken and triturated with potassium bromide. The

(Table no. 04) Interpretation for IR spectrum of allyl sucrose

Sample	Assignment	Wave number (cm ⁻¹)
Allyl sucrose	C=C-H vibration	925
	C=C-H vibration	995
	C-O vibration	1077
	C=C vibration (Alkene)	1647
	O-H vibration	3560

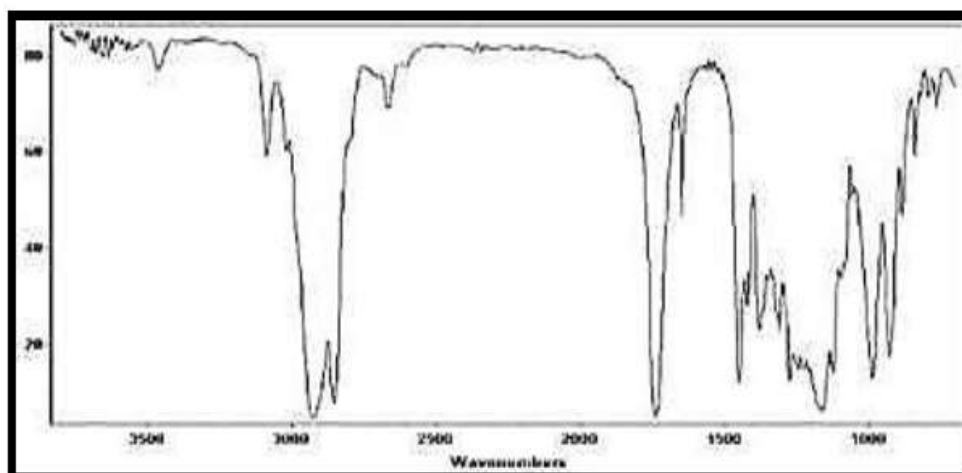


Table 05. The optimized batch of the polymer

Formulation code	Monomer: Cross-linker (g:g)	Initiator (g)	Solvent (Porogen)	Water swelling capacity (g of water/1g of polymer)	% Yield
P11	9.0:1.0	0.075	Chloroform	265	92

**Characterization of monomer: -
Physical characteristics**

Physical characteristics of monomers.

Monomer	Boiling point	Appearance	Solubility
Methacrylic acid	160 ⁰ C-162 ⁰ C	Colorless liquid	Soluble in water, alcohol, chloroform, esters.
Acrylic acid	140 ⁰ C-142 ⁰ C	Colorless liquid	Soluble in water, alcohol, chloroform, esters.

IR spectral study:- Methacrylic acid:-

Procedure: About 2mg of methacrylic acid was weighed and triturated with potassium bromide. The powder was then placed in dye cavity of pellet

machine and 10psi pressure was applied. The prepared potassium bromide pellet was kept in IR cell and results were recorded

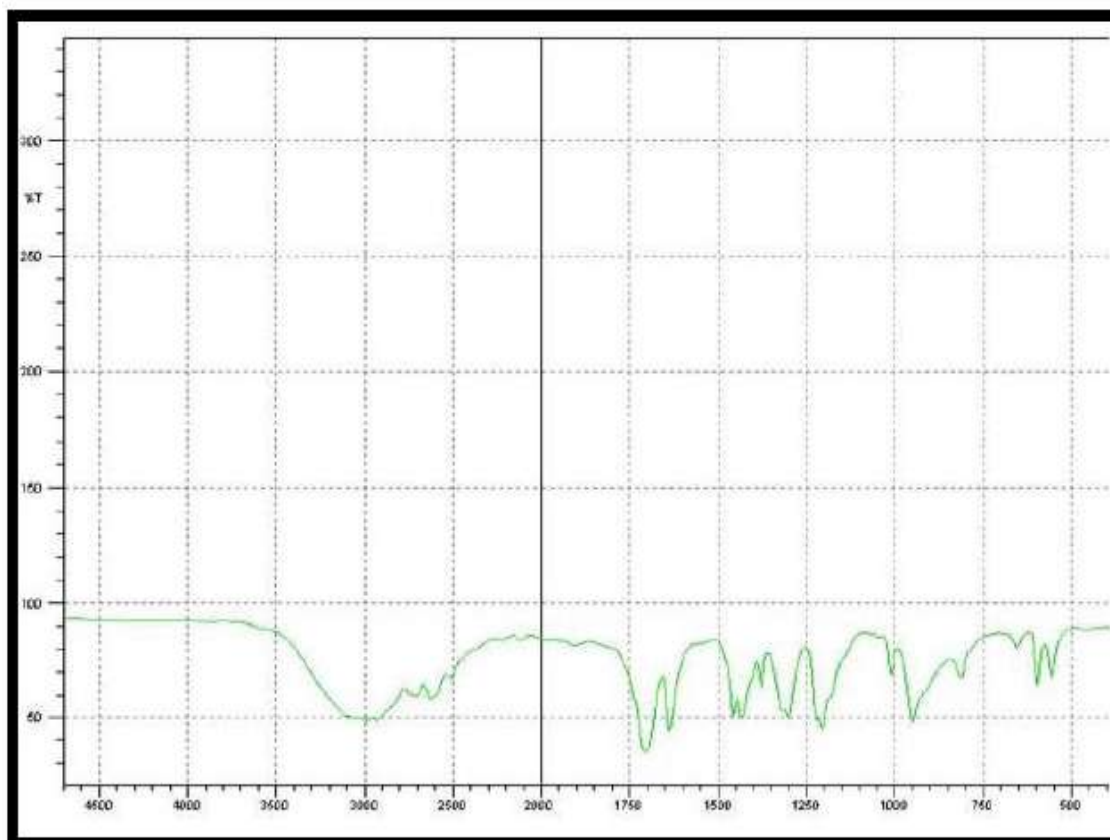


Figure IR spectrum of methacrylic acid.

Interpretation: An IR spectrum of methacrylic acid shows C-H stretching vibration of alkane occurs at 2840cm⁻¹ and a symmetrical bending vibration at 1650cm⁻¹. Another band at 1320-1210cm⁻¹ is due to C-H stretching and O-H bending vibration of carboxylic acid. Broad intense band at 3560cm⁻¹ indicate presence of -OH group at carboxylic acid.

Acrylic acid:-

Procedure: About one drop of Acrylic acid was taken and triturated with potassium bromide. The powder was then placed in dye cavity of pellet machine and 10psi pressure was applied. The prepared potassium bromide pellet was kept in IR cell and results were recorded

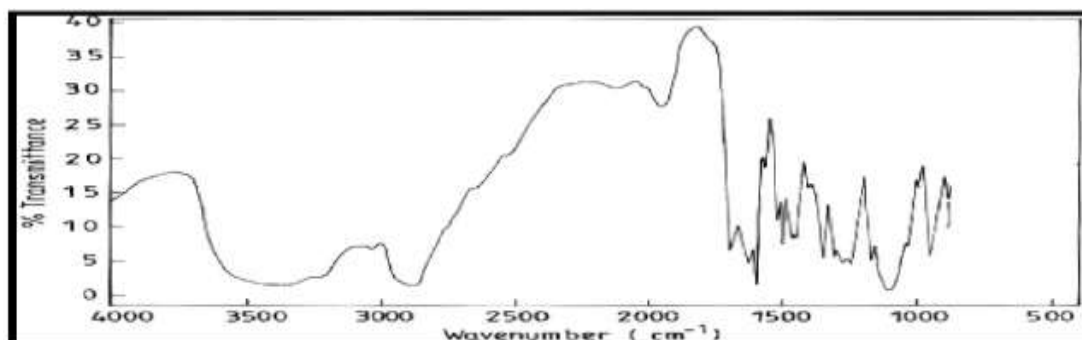


Figure IR spectrum of acrylic acid

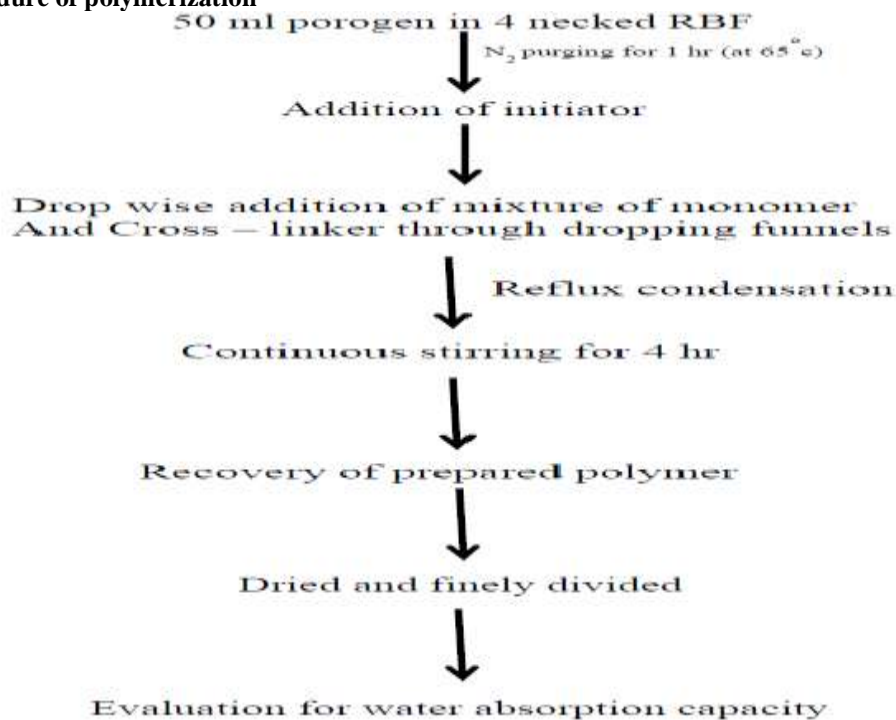
Interpretation: An IR spectrum of acrylic acid shows band at $1320\text{-}1210\text{cm}^{-1}$ is due to C-H stretching and O-H bending vibration of carboxylic acid. Broad intense band at 3560cm^{-1} indicate presence of -OH group at carboxylic acid.

Preparation of polymer

Description of assembly The assembly consists of a 250 ml four necked round bottomed flask equipped with teflon blade attached through a

glass rod to the electrical motor with a regulator. The rod passes through the teflon bush attached to the central neck of the flask. A thermometer was placed in the thermowell attached to the second neck of the flask. Third neck was attached to the condenser, while through the fourth neck glass tube was connected to a Nitrogen cylinder via rubber tubing through a regulator. The round bottom flask was kept on a heating mantle equipped with thermostat for temperature regulation.

General procedure of polymerization



Evaluation of prepared polymer

In vitro water absorbent capacity of polymers

The polymers obtained in each batch were dried properly and crushed to finer particle size.

The powdered polymers were passed through #200 sieve to obtain uniform particles of polymer.

To study the quantity of water absorbed, 1 g of each polymer was taken in a conical flask and a measured amount of distilled water (200 ml) was

added to it. The polymers were allowed 4-5 hour for complete swelling, then the swelled polymers were passed through #200 sieve.^[73]

The quantity of water collected below the sieve was measured and amount of water absorbed by 1 g of polymer was calculated.

Optimization of initiator concentration The synthesis of water swellaible polymer was carried out in chloroform as solvent. Method involves, 50ml solvent was taken in four necked round bottom flask of 250ml capacity and subjected to continuous N₂ purging for 1 hr at 65⁰C. After 1 hr

of N₂ purging, benzoyl peroxide was added as initiator in different conc.(0.025g, 0.05g, 0.075g, 0.1g) (Table 13). Afterward mixture of acrylic acid as monomer and allyl sucrose as cross-linker was added drop wise into above round bottom flask in constant monomer to cross-linker concentration ratio(8.0:2.0). This solution was stirred under reflux for 4 hr at 61⁰C. After 4 hr, solid product was removed filtered, dried at 61⁰C in the hot air oven, powdered and subjected to evaluation. And the observations were noted for different concentration of initiators as shown in table

Formulation code	Monomer : Cross-linker (g:g)	Initiator (g)	Solvent (Porogen)
I1	8.0:2.0	0.025	Chloroform
I2	8.0:2.0	0.05	Chloroform
I3	8.0:2.0	0.075	Chloroform
I4	8.0:2.0	0.100	Chloroform

Table 07. Water swelling capacity and %yield for the batches of different initiator concentrations

(Table no. 08)

Formulation code	Initiator (g)	Water swelling capacity (g of water/1g of polymer)	% Yield
I1	0.025	75	83
I2	0.05	110	86
I3	0.075	125	91
I4	0.1	90	79

On the basis of result soft water swelling capacity for different initiator concentration; it was found that, batch I3 with 0.075g of initiator shown maximum water swelling capacity 125 as compared to batch I1, I2 and I4 with water swelling capacity 75, 110 90 (g/1g) respectively . Hence, 0.075 g of initiator concentration was optimized and carried for further selection of monomer.

Selection of monomer

Above optimized batch was taken for selection of monomer at constant monomer: cross-linker concentration ratio (8.0:2.0), 0.075g of initiator and chloroform as a solvent for acrylic acid and methacrylic acid as monomer shown in table 15. And the observations were noted for water swelling capacity and % yield.

Formulation code	Monomer: Cross-linker (g:g)	Initiator (g)	Solvent (Porogen)	Monomer	Water swelling capacity (g of water/1g of polymer)
M1	8.0:2.0	0.075	Toluene	Acrylic acid	Bulk formation
M2	8.0:2.0	0.075	Chloroform	Methacrylic acid	125

Table 09. Water swelling capacity and % yield for different batches of monomer:cross-linker concentration ratio

Formulation code	Monomer: Cross-linker (g:g)	Water swelling capacity (g of water/1g of polymer)	% Yield
P1	10.0:0.0	Soluble in water	80
P2	9.9:0.1	Soluble in water	87
P3	9.8:0.2	Soluble in water	82
P4	9.7:0.3	Soluble in water	80
P5	9.6:0.4	Soluble in water	83
P6	9.5:0.5	Partially Soluble in water	84
P7	9.4:0.6	Partially Soluble in water	81
P8	9.3:0.7	Partially Soluble in water	85
P9	9.2:0.8	Partially Soluble in water	85
P10	9.1:0.9	Partially Soluble in water	88
P11	9.0:1.0	265	92
P12	8.9:1.1	241	89
P13	8.8:1.2	228	90
P14	8.7:1.3	215	92
P15	8.6:1.4	193	92
P16	8.5:1.5	179	89
P17	8.4:1.6	168	85
P18	8.3:1.7	156	82
P19	8.2:1.8	146	91
P20	8.1:1.9	138	90
P21	8.0:2.0	125	89

IR spectral study of prepared polymer

About 1 mg of polymer (P11) was ground with potassium bromide and then pellet was prepared

using Potassium bromide press. Scanning was performed between the range 4000-500 cm⁻¹. The peaks are shown in Fig

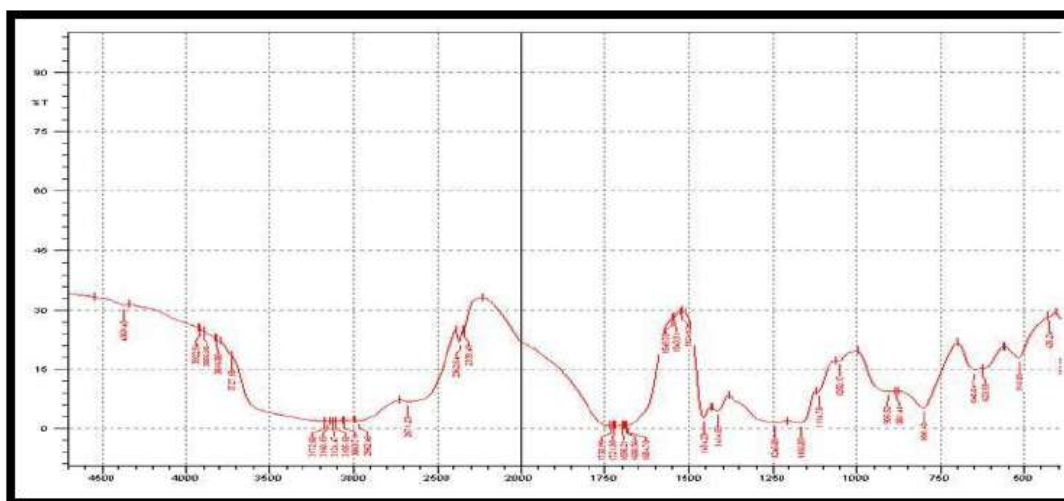


Table 10. Interpretation for IR spectrum of prepared polymer

Sample	Assignment	Wave number (cm ⁻¹)
Polymethacrylate polymer	=CH stretching	3206
	C-O-C stretching (ether)	1166
	C=O stretching (Acid)	1721
	OH stretching	2962
	=CH vibration	1357
	Acrylate	1246
	CH ₃ bending	1414
	Ar and ene	800

III. RESULT AND DISCUSSION

7.1. Synthesis of cross-linker

Allyl sucrose as a cross-linker was selected because it has good hydrophilicity as well as hydrophobicity. The cross-linker allyl sucrose was synthesized by converting sucrose into sodium sucrose and then by reacting it with allyl bromide to obtain product allyl sucrose. The synthesized product was characterized by properties like boiling point, appearance, solubility and FTIR spectral analysis. And the TLC was carried out for the synthesized product, it showed single spot for the sample, therefore synthesized product was found to be pure.

Synthesis of water swellable polymer

Optimization for initiator, monomer, solvent and monomer: cross-linker concentration ratio

The monomer acrylic acid and methacrylic acid were selected for the preparation of water swellable polymer. Acrylic acid showed lump formation on polymerization, it may be because of moisture content (8.25%) as shown in table 12, when methacrylic acid was used as monomer; it produced free flowing powder form on polymerization. Hence methacrylic acid was selected for further studies (Table 15). The monomer methacrylic acid was characterized for physical, spectral analysis and moisture content with assay. All these values were found to be within limits.

The water swellable polymer was prepared by optimizing initiator concentration (Table 14). The initiator (benzoyl peroxide) was optimized in the concentration of 0.075g having 91% of percentage yield (batch I3) and showed water swelling capacity of 125g/g as compared to 0.025g (batch I1) , 0.05g(batch I2) and 0.1g(batch I4) with water swelling capacity of 75g/g, 110g/g and 90g/g respectively. At low concentration of initiator, few numbers of chains are initiated

leading to the formation of longer polymer chain length and higher molecular weight polymer with high water swelling capacity. The concentration of initiator is inversely proportional to the molecular weight of polymer. Increasing the concentration of initiator, i.e. higher number of free radical initiates the larger number of small chains forming lower molecular weight polymer results in an increase in the water swelling capacity. At 0.1g of benzoyl peroxide, low water swelling capacity, and partial water solubility was observed because of very small particles of polymer with low cross-linking.^[80]

Chloroform solvent system was selected for the preparation of water swellable polymer (Batch S2) on the basis of maximum water swelling capacity with 125g/g and 91% of percentage yield as compared to toluene (Batch S1) and ether (Batch S3) with water swelling capacity of 88g/g and 95g/g respectively as shown in table 17. Where reaction were carried out at 111^oC, 80^oC and 61^oC for toluene, ether and chloroform respectively under reflux.

Monomer: cross-linker ratio was optimized in the concentration ratio of 9.0:1.0 (Batch P 11) on the basis of maximum water swelling capacity with 265g/g and 94% of percent yield as compared to batch P10 (1.0:9.0) which was partially soluble in water and P12 (8.9:1.1) with water swelling capacity 241g/g, which is shown in table 21. Where batch P1 (10.0:0.0), P2 (9.9:0.1), P3 (9.8:0.2), P4 (9.7:0.3), P5 (9.6:0.4) were soluble in water, batch P6 (9.5:0.5), P7 (9.4:0.6), P8 (9.3:0.7), P9 (9.2:0.8), P10 (9.1:0.9) were partially soluble in water, this may be because of the cross-linking between long polymer chain at very low extent that couldn't make it hydrophilic and absorb the water to swell, solvent diffuses into the solid, allowing space for movement and then slow longitudinal diffusion of solvent allows single chains to dissolve. Batch P12 (8.9:1.1), P13 (8.8:1.2), P14 (8.7:1.3), P15 (8.6:1.4), P16

(8.5:1.5), P17 (8.4:1.6), P18(8.3:1.7), P19 (8.2:1.8), P20 (8.0:2.0) and P21 (8.0:2.0) showed water swelling capacity 265g/g, 241g/g, 228g/g, 215g/g, 193g/g,173g/g, 168g/g, 156g/g, 146g/g, 138g/g and 125g/g respectively. The decrease in water swelling capacity from the batch P11(9.0:1.0) to P21(8.0:2.0) with increase in cross-linker concentration was may be due to the higher cross-linking and increase in the cross-linking density or cross-linking network causing the linking of polymer chains in the structure, decrease in distance between cross-linking points results into low water swelling capacity. And at the intermediate concentration of cross-linker i.e. P11 (9.0:1.0) showed maximum water swelling capacity, because of optimum cross-linking and hydrophilicity counter balancing the action of each other.^[81,82,83]

Spectral analysis of prepared water swellable polymer showed the presence of C-O-C ether linkage at wave number 1106cm^{-1} which implied monomer-cross linker linkage and CH_2 stretching at wave number 3206cm^{-1} implied that monomer-monomer linkage (Table No. 23) confirmed the structure of prepared water swellable polymer. Batch P11 having initiator concentration 0.075g, chloroform as a solvent and monomer: cross- linker ratio 9.0:1.0 was considered for the preparation of drug delivery system i.e. gel (Table 22).

Each molecule can be represented by parallel rows of the principal atoms with periodical bridging links between them. When water comes into contact with these rows an electrical repulsion between rows is generated, as in the poles of magnet, and the rows move apart. This draws more water into the molecule and the rows move further apart. This results in a rapid swelling of each particle.

IV. SUMMARY AND CONCLUSION

It can be concluded that, the water swellable polymer was prepared by using synthesized cross-linker (allyl sucrose). The water swelling capacity of the prepared water swelling polymer was affected by changing the monomer, initiator concentration, solvent and monomer to

cross-linker concentration ratio, used in the polymerisation process. Optimized batch P11 with methacrylic acid as a monomer, monomer to cross-linker concentration ratio (9.0g:1.0g), initiator (0.075g) and chloroform as a solvent, showed maximum water absorption capacity among all the batches.

Overall, from the present work, it may be concluded that the prepared water swellable polymer will be potential carrier for the drug delivery system.

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