Available Online at

http://www.ijcpa.in

October-December 2017

International Journal of CHEMICAL AND PHARMACEUTICAL ANALYSIS

eISSN: 2348-0726 ; pISSN : 2395-2466

Research Article | Volume-5 | Issue-1 | Article ID: 1362

SYNTHESIS OF POLYMERS BY MICROWAVE IRRADIATION AND CHARACTERIZATION FOR TASTE MASKING

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Received: 27 July 2017 / Revised: 15 September 2017 / Accepted: 25 November 2017 / Available online 31 December 2017

ABSTRACT

Polymers have been used as a main tool to control the drug release rate from the formulations and for its taste masking ability. Polymers were synthesized using 4-vinyl pyridine (4-VP), 2-hydroxy ethyl methacrylate (HEMA), methacrylic acid (MA), and methyl methacrylate (MMA) using free radical chain growth polymerization in microwave synthesis system. Characterization of polymers was done on various parameters of viscosity, solubility, molecular weight etc. The result revealed that the synthesized polymers are able to mask the taste of some bitter drugs like Cefuroxime axetil (CA), Cefpodoxime proxetil (CP) and Cefixime.

Keywords *– Polymer; Taste masking; Microwave; Cefuroxime axetil ; Cefpodoxime proxetil ; Cefixime.*

1. INTRODUCTION

A substance that has a molecular structure built up chiefly or completely from a large number of similar units bonded together is called as polymers. Polymers have been used as a main tool to control the drug release rate from the formulations.

Extensive applications of polymers in drug delivery have been realized because polymers offer unique properties which so far have not been attained by any other materials. Advances in polymer science have led to the development of several novel drug-delivery systems. A proper consideration of surface and bulk properties can aid in the designing of polymers for various drug-delivery applications. These newer technological developments include drug modification by chemical means, career-based drug delivery and drug entrapment in polymeric matrices or within pumps that are placed in desired bodily compartments. These technical developments in drug delivery/targeting approaches improve the efficacy of drug therapy thereby improve human health.

Polymer chemists and chemical engineers, pharmaceutical scientists are engaged in bringing out design predictable, controlled delivery of bio active agents. Biodegradable polymers have been widely used in biomedical applications because of their known biocompatibility and biodegradability[1].

Advances in polymer science have led to the development of novel delivery systems. The introduction of new polymers has resulted in development of polymers with unique properties. Initially polymers were used as solubilisers, stabilizers and mechanical supports for sustained release of drugs. But over a period of time, the functionalities of polymers have changed. The polymers have been synthesized to suit specific needs or rather solve specific problems associated with development of drug delivery systems. So, there is need to understand the role of polymers.[2]

The pharmaceutical applications of polymers range from their use as binders in tablets to viscosity and flow controlling agents in liquids, suspensions and emulsions. Polymers can be used as film coatings to mask the unpleasant taste of a drug, to enhance drug stability and to modify drug release characteristics.

2. MATERIALS AND METHODS

All the chemicals used were of analytical grade purchase from Himedia, Loba and sigma Aldrich Bangalore. CA, CP and Cefixime were received as a gift sample from ZIM lab Kalmeshwar, Nagpur. Polymers were synthesized by bulk polymerization using different compositions of monomer as given in table 1 and 2.

2.1 Procedure for synthesis of polymer[3,4,5]

pH sensitive polymers were synthesized in microwave synthesis system. Monomers methyl methacrylate, 4- Vinyl pyridine, 2-Hydroxy ethyl methacrylate and methacrylic acid were mixed together and an azo inhibitor, azo bis isobutyronitrile 1% w/w of total monomer was added. Reaction mixture was purged with nitrogen gas to provide inert atmosphere. Polymerization reaction was carried out at power level 3 (240W) for 30 min. polymers so synthesized were recovered by dissolving in solvent mixture comprising dichloromethane and methanol (1:1) and later precipitated in water.

Different monomers were selected for this synthesis. Table 1 gives the ranges of different polymers that were varied during synthesis. Composition of all the polymers is given in table 2, Fig. 1 gives the general scheme for synthesis of polymers.

Table 1: Monomers and their compositons for polymer synthesis

Monomer's code	Monomers	Range (%)
A	4- Vinyl pyridine	2.5-10
B	2- hydroxyl ethyl methacrylate	5-27.5
C	Methacrylic acid	5-20
D	Methyl methacrylate	42.5-87.5

Table 2: Compositions of monomer used for the synthesis of polymer

Product code	A (%)	B (%)	C (%)	D (%)	Total
1	2.5	5	5	87.5	**100**
2	10	5	5	80	**100**
3	2.5	27.5	5	65	**100**
4	2.5	5	20	72.5	**100**
5	10	27.5	5	57.5	**100**
6	10	5	20	65	**100**
7	2.5	27.5	20	50	**100**
8	10	27.5	20	42.5	**100**

2.2 Scheme

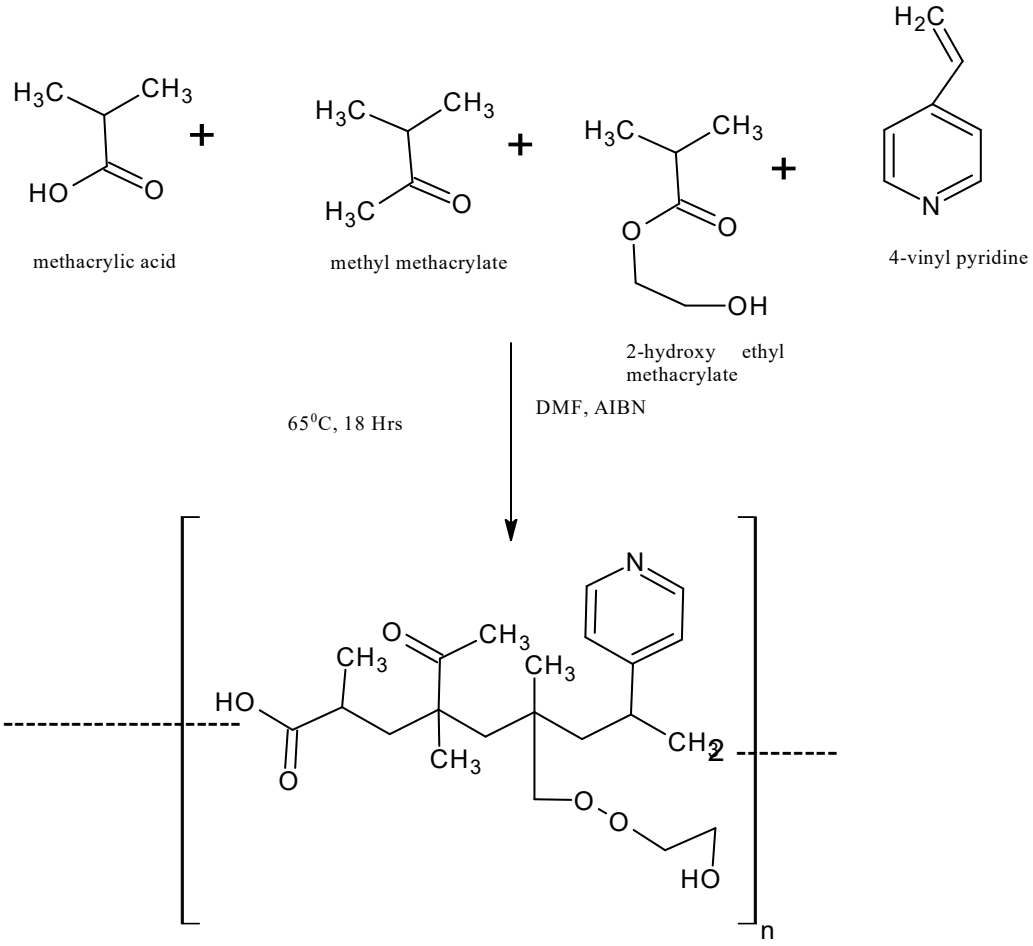

Fig. 1: Scheme for synthesis of polymers

2.3 Characterization of polymers

Solubility of all polymers in various organic solvents was study by shake flask method. Melting point of synthesized polymers was determined by capillary method. Viscosity was determined by Ostwald's viscometer. Molecular weight determined by using viscosity method, Mark- Houwink equation was used to calculate molecular weight of polymer using known value of intrinsic viscosity. Flow properties (bulk and tapped density) were also measured. Loss on drying by using hot air oven was obtained.

2.4 Formulation

Taste masked microcapsules of Cephalosporins antibiotic CA were obtained by microencapsulation by emulsification solvent evaporation technique. 2.0 g of CA was dissolved in polymer solution containing 6.0 g of polymer in 40 ml of mixture of methanol and dichloromethane (1:1). The nonionic surfactant span 85 was added 0.5 % w/w to facilitate the dispersion of CA in the polymer solution. The dispersion of CA was added dropwise to the bath of light liquid paraffin under mechanical stirring. A constant mechanical stirring rate of 1000 rpm and at a room temperature was maintained for 3-4 hours. Solvent was allowed to evaporate and the microspheres so obtained were separated by filtration, washed by petroleum ether and dried at 27 ^{o}C. Under vacuum for 24 hours. [6] Microsphers of Cefpodoxime proxetil and Cefexime were prepared by using the same procedure used for CA.

2.5 Gustatory Sensation Test

Gustatory sensation test was carried out according to the method described by Mou-ying et al[7-15]. Twenty healthy human volunteers, of either sex, in the age group of 23– 27 years were selected based on quinine taste sensitivity test. The non-taster and super tasters were rejected. Binary systems equivalent to 1 g of CA was dispersed in 100 ml of water for 15 s. For comparison pure CA was subjected to taste evaluation by the panel. Immediately after preparation, each volunteer held about 1 ml of the dispersion in the mouth for 30 s. After expectoration, bitterness level was recorded. A numerical scale was used with the following values: 0 = tasteless, 0.5 = very slightly bitter, 1 = slightly bitter, 1.5 = slight to moderate bitter, 2 = moderately bitter, 2.5 = moderate to strong bitter, 3 = strongly bitter, 3+ = very strong. This numerical scale was validated by testing samples randomly. The oral cavity was rinsed with distilled water three times to avoid bias. Wash out period between testing different samples was 15 min. The threshold of bitterness was determined as point at which maximum number of the volunteers described the taste as bitter or slightly bitter.

3. RESULTS AND DISCUSSION

Most of the synthesized polymers were white in color and amorphous in nature. Synthesized polymers were slightly soluble in water, sparingly soluble in methanol, soluble in dichloromethane, acetone, DMF and DMSO, freely soluble in methanol: dichloromethane (2:1). Average molecular weight of polymers was 168^0 C. viscosity of all polymers ranges from 0.5541 to 0.610. Molecular weight was ranges from 3288851.630 to 435712.224. All polymers show highest value for Carr's index and Hausner's ratio and shows good flow properties. Our titled compounds are known to possess taste masking properties.

4. CONCLUSION

Synthesized polymers were characterized physico- chemically which shows that polymers were synthesized as per specifications. After synthesis it is characterize for its taste masking ability, which reveals that these polymers have good taste masking ability.

Taking into consideration it is concluded that:

1) Acid insoluble polymers could be synthesized with the help of microwave irradiation.
2) Synthesized polymers were found to be successful in masking bitter taste of drug like Cefuroxime axetil.

REFERENCES

1. Raizada A, Bandari A, Kumar B. Polymers in drug delivery: a review. Int. J. Pharm. Res. Dev. 2010;2(8):9-20.
2. Kadajji V.G., Betageri G.V. Water Soluble Polymers for Pharmaceutical Applications, Polymers. 2011,3, 1972-2009.
3. Furniss BS. Vogel's textbook of practical organic chemistry. Pearson Education India; 1989.
4. Menjoge A. R, Kulkarni M.G. designing a self-associated cationic polymer for enhanced compatibility, palatability, and gastric release of Cefuroxime axetil. Biomacromolecules. 2007, 10, 1-11.
5. Rowe RC, Sheskey PJ, Owen SC, editors. Handbook of pharmaceutical excipients. London: Pharmaceutical press; 2006.
6. Kulkarni et al, taste masked pharmaceutical composition comprising bitter drug and pH sensitive polymer, patent no: US 2005/0136114 A1.
7. Guohua Jiang, Li Wang, Tao Chen, Haojie Yu, Xiaochen Dong, Chang Chen, Synthesis and self-assembly of hyperbranched polyester peripherally modified by touluene-4-sulfonyl groups, Polymer. 2005, 46, 9501–9507.
8. Kulkarni et al, pH sensitive polymers and process for preparation thereof, patent nm: US 7,531,612,B2.

9. Shah PP, Mashru RC. Development and evaluation of artemether taste masked rapid disintegrating tablets with improved dissolution using solid dispersion technique. Aaps Pharmscitech. 2008;9(2):494-500.
10. Kazuhiro Sugamura Mitsubishi Gas Chemical Company, Inc.SIDS Initial Assessment Report for SIAM 14, date for circulation 1 Feb. 2002 (Paris, 26-28 March 2002).
11. Determan MD, Cox JP, Seifert S, Thiyagarajan P, Mallapragada SK. Synthesis and characterization of temperature and pH-responsive pentablock copolymers. Polymer. 2005;46(18):6933-46.
12. Mohan G.Kulkarni and Anupa R. Menjoge, Maharashtra (IN) CSIR, New Delhi (IN), pH sensitive polymers and process for preparation thereof,US 7,531,612 B2, May 12,2009.
13. Ayenew Z, Puri V, Kumar L, Bansal AK. Trends in pharmaceutical taste masking technologies: a patent review. Recent patents on drug delivery and formulation. 2009 Jan 1;3(1):26-39.
14. Vummaneni V, Nagpal D. Taste masking technologies: an overview and recent updates. International Journal of Research in Pharmaceutical and Biomedical Sciences. 2012 Apr;3(2):510-24.
15. Evoniv industries Evonik Röhm GmbH Pharma Polymers Kirschenallee 64293 Darmstadt, www.evonik.com (Accessed on July 27, 2012).