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Synthesis and characterization of multifunctional polymers bearing active ingredients

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ABSTRACT

The synthesis of poly(epichlorohydrin) was investigated using ring opening polymerization of epichlorohydrin amorced with perchloric acid in dichloromethane in the presence of methanol at 35 °C. The chemical modification of the obtained polymer was performed using the phase transfer method, by reacting poly (epichlorohydrin) with acetylsalicylic acid (ASA) then with menthol in an aqueous sodium hydroxide solution in the presence of tetrabutylammonium hydrogensulfate (TBAH). The obtained polymers were characterized by FT-IR spectroscopy and ^1H NMR.

Keywords: active ingredient, multifunctional polymer, poly(epichlorohydrin), ring opening polymerization.

INTRODUCTION

The synthesis of multifunctional polymers have attracted much attention in recent years [1] thanks to their many applications, such as their use as precursors for the preparation of grafted copolymers [2] or three-dimensional networks such as hydrogels [3], as antimicrobial and drug delivery in the pharmaceutical field [4,5], as biocidal in agriculture [6]. The use of this kind of polymers in the pharmaceutical industry as drug molecules carriers or vectors of active ingredients have attracted great scientific because they are widely used in various applications [7,8]. For that several techniques of synthesis of these polymers can be envisaged: (a) The dispersion of drug (active ingredient) in a polymer or copolymer matrix, which is then shaped plates, spheres or capsules [9,10], (b) The preparation of a monomer bearing the active ingredient, followed by polymerization or copolymerization as appropriate. (c) Finally, the attachment (grafting) of the drug molecule to a macromolecule through labile bonds [11].

This paper reports the last technique, grafting of active ingredient as acetylsalicylic acid and menthol onto poly(epichlorohydrin). This last is an important polymer that has a reactive chloro methyl group and it is easily converted to various functional polymers. Furthermore, poly (epichlorohydrin) is hydrophilic, atoxic biocompatible and biodegradable polymer; it is used in pharmaceutical [12], cosmetics and textiles [13]. A chemical modification method was adopted by grafting acetylsalicylic acid and menthol onto polyepichlorohydrin homopolymer using the phase transfer method.

MATERIALS AND METHODS

Materials: epichlorohydrin (ECH) monomer was purchased from Aldrich and distilled under reduced pressure; dichloromethane and methanol were distilled on the day of experiment, perchloric acid, menthol and acetylsalicylic acid.

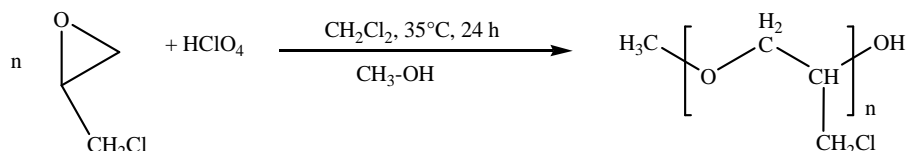
Measurements: FT-IR spectra was obtained on ALPHA FT-IR mark "Bruker" bearing the Module "Platinum diamond ATR single reflection ATR", at room temperature in the range of 400 – 4000 cm^{-1} . ^1H NMR spectra was

recorded on a Bruker Avance AV 400 MHz spectrometer in deuterated chloroform. The chemical shifts were reported in parts per million (ppm) downfield from tetramethylsilane (TMS).

RESULTS AND DISCUSSION

Synthesis of poly (epichlorohydrin) (PECH)

The ring opening of epichlorohydrin (ECH) was performed in dichloromethane, using perchloric acid in the presence of methanol at 35 °C under a nitrogen atmosphere and magnetic stirring for 24 hours, according to the reaction scheme 1.



Scheme 1: ring opening polymerization of epichlorohydrin

The obtained polymer was precipitated in cyclohexane at room temperature to remove the unreacted monomer and other impurities. The precipitate, was dried under vacuum, the experimental conditions of the ring opening polymerization are summarized in Table 1.

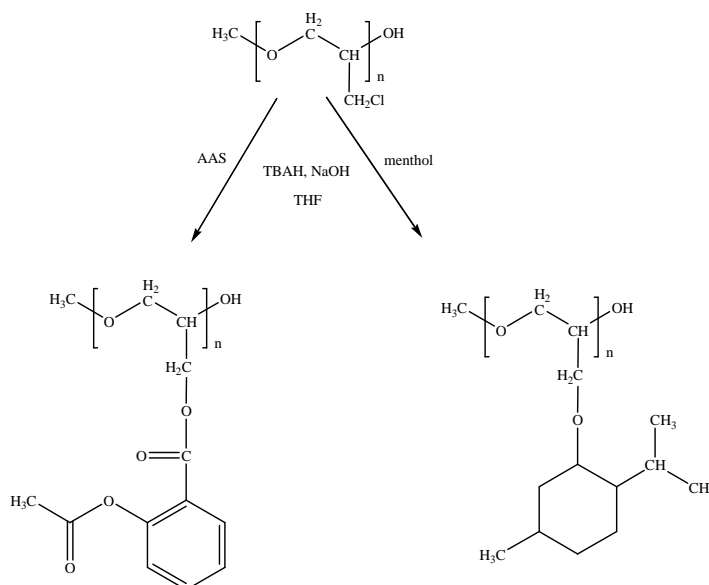
Table 1 Experimental conditions of the cationic polymerization of PECH

[ECH] (mol/l)	[HClO ₄] (mol/l)	[CH ₃ OH] (mol/l)	Rdt (% weight)
11.24	1.12	1.02	91

Chemical modification of poly (epichlorohydrin) by grafting acetylsalicylic acid (ASA) and menthol

The principle of this grafting is illustrated by the diagram below (scheme 2). It is a substitution reaction of chlorine atoms of poly (epichlorohydrin) located along the polymer chain, by hydroxyl groups of menthol and acetylsalicylic acid.

The chemical modification of poly (epichlorohydrin) was performed using the phase transfer method, by reacting poly (epichlorohydrin) with acetyl salicylic acid (ASA) and menthol in an aqueous sodium hydroxide solution in the presence of tetrabutylammonium hydrogensulfate (TBAH), with magnetic stirring at 25 °C in THF. The experimental conditions are summarized in Table 2.



Scheme 2 chemical modification of poly (epichlorohydrin) by grafting aspirin and menthol

The chemical modification of poly (epichlorohydrin) was performed using the phase transfer method, by reacting poly (epichlorohydrin) with acetylsalicylic acid (ASA) then menthol in an aqueous sodium hydroxide solution in the presence of tetrabutylammonium hydrogensulfate (TBAH), with magnetic stirring at 25 °C in THF. The experimental conditions are summarized in Table 2.

Table 2 Experimental conditions of obtained polymers PECH-g-ASA and PECH-g-menthol

[PECH] (mole/l)	[AAS] (mole/l)	[NaOH] (mole/l)	[TBAH] (mole/l)	THF (ml)	T (°C)	T (%)	Rdt
PECH-g-ASA	0.410	0.414	0.63	0.4120	25	67.87	
PECH-g-menthol	0.42		0.425	0.42	20	25	56.12

Characterization of obtained polymers

FTIR measurement

PECH: 3419 cm^{-1} (O-H of water), 2962- 2872 cm^{-1} (CH, CH_2), 1098 cm^{-1} (C-O-C), 751 cm^{-1} (CCl)(Fig.1).

PECH-g-ASA: 1635 cm^{-1} (C=O), 1588 cm^{-1} (C=C), 1387 (O-C = O) (fig.2).

PECH-g-menthol: 1460 cm^{-1} (CH of menthol rings), 1101 cm^{-1} (C-O-C) (fig.3)

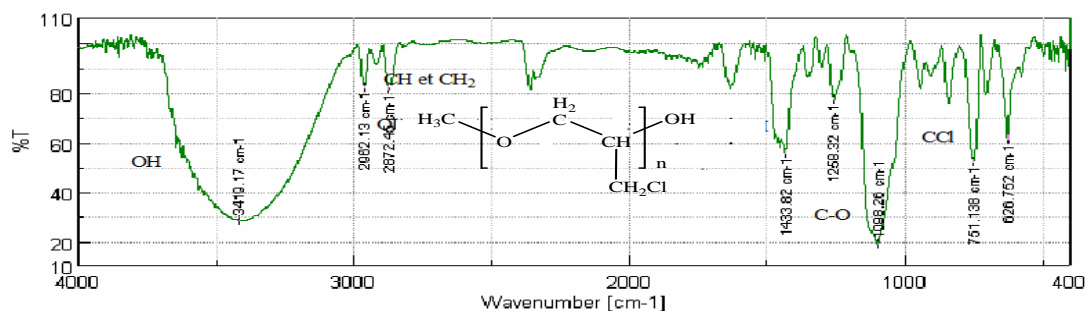


Fig. 1: FTIR spectrum of poly (epichlorohydrin) homopolymer

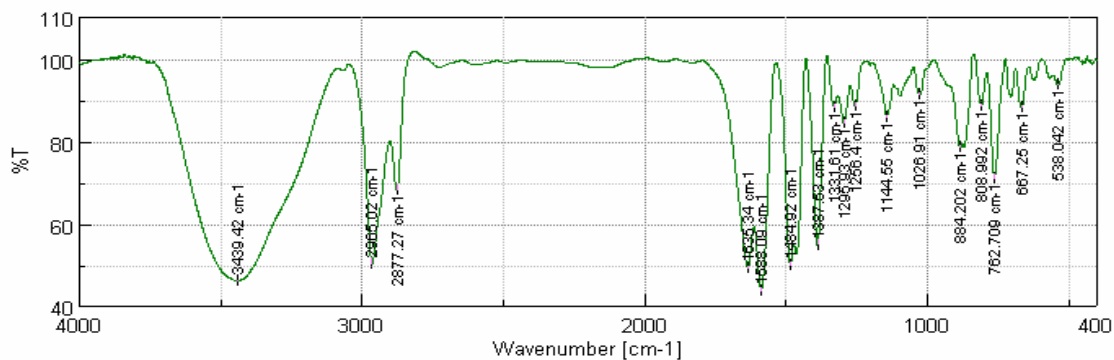


Fig. 2: FTIR spectrum of poly (epichlorohydrin) -g- ASA

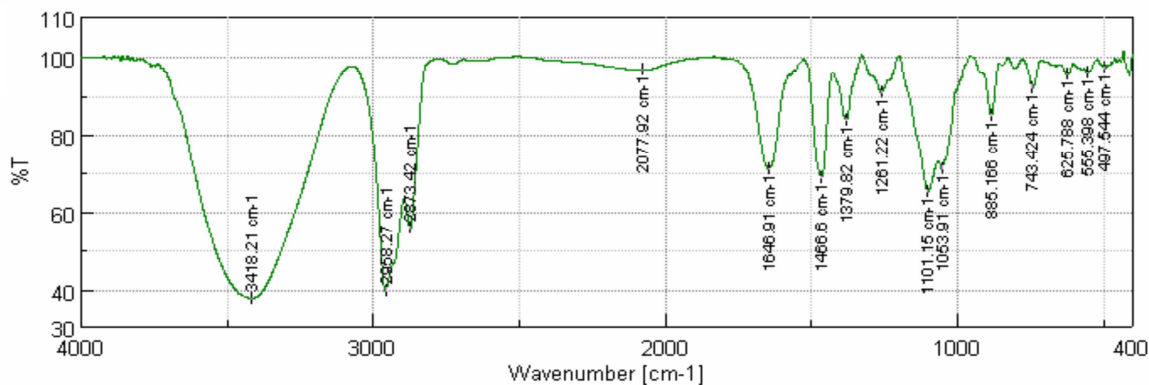


Fig. 3: FTIR spectrum of poly (epichlorohydrin)-g- menthol

Examination of FTIR spectra of poly (epichlorohydrin)-g-ASA and poly (epichlorohydrin)-g-menthol respectively (Fig 2 and Fig 3) have enabled us to determine, first, the disappearance of the characteristic band of CH_2Cl group located at 751cm^{-1} .

In Fig 2, the spectrum has allowed us to observe the appearance of new bands characteristic of the elongation vibration of carbonyl groups, ethylene group respectively located at 1635 and 1588cm^{-1} and absorption bands located at 762 and 884cm^{-1} corresponding to the deformations of the CH and $-\text{CH}_2$ bonds belonging to the benzene rings, as well as band characterizing the ester bond $\text{O}-\text{C}=\text{O}$ located at 1387cm^{-1} .

Furthermore, the spectrum in (Fig 3), there is appearance of a new absorption band at 1460cm^{-1} characteristic deformation of the cyclic CH bonds belonging to menthol cycle grafted on poly (epichlorohydrin) homopolymer and the vibration of the bond $\text{C}-\text{O}-\text{C}$ at 1101cm^{-1} .

These results allow us to conclude that there was grafting of acetyl salicylic acid and menthol respectively on poly (epichlorohydrin) homopolymer using the phase transfer method, thus leading to the formation of multifunctional polymers with active ingredients.

¹H NMR measurement

Fig. 4 showed ¹H NMR spectra of poly (epichlorohydrin) homopolymer before grafting active principles, poly (epichlorohydrin)-g- acetylsalicylic acid and poly (epichlorohydrin)-g- menthol are shown respectively in fig.5 and fig.6. ¹H NMR results confirmed that the active ingredients were grafted successfully onto poly (epichlorohydrin) homopolymer as shown by disappearance of the characteristic peaks of chloromethylene protons (CH_2Cl) at 3.5 ppm, and by formation of new peaks of characteristics protons of each active principle 7.59 ppm - 6.89 ppm of benzene rings of acetylsalicylic acid and 1.53 ppm - 2.08 ppm corresponds to menthol rings.

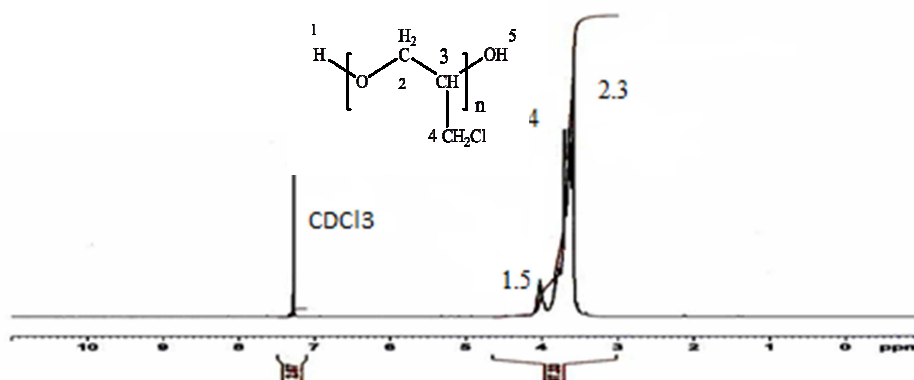


Fig. 4: ¹H NMR spectrum of poly (epichlorohydrin) homopolymer

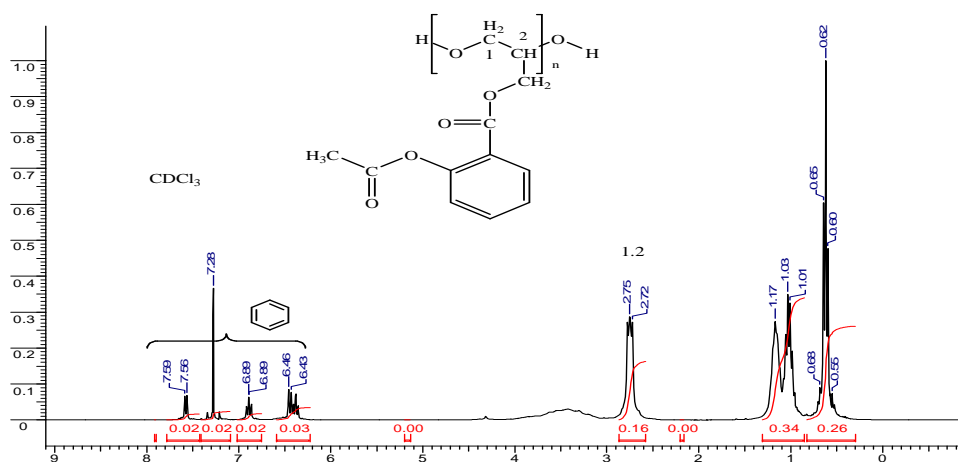


Fig. 5: ¹H NMR spectrum of poly (epichlorohydrin)-g-ASA

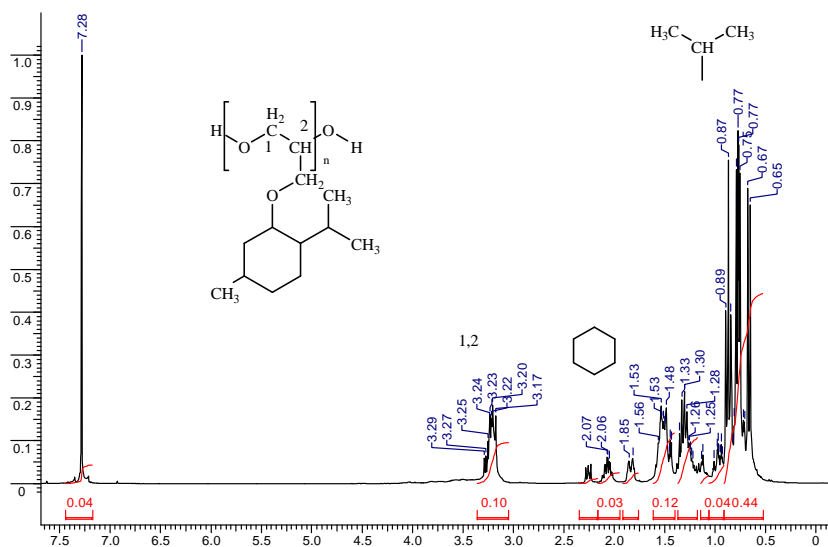


Fig. 6: ^1H NMR spectrum of poly (epichlorohydrin)-g-menthol

CONCLUSION

A novel multifunctional polymer as poly (epichlorohydrin) grafted acetylsalicylic acid and menthol were successfully prepared using the phase transfer method. The structures of the obtained polymers were confirmed with FT-IR and ^1H NMR analysis.

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