

SYNTHESIS AND CHARACTERIZATION OF POLY ESTER AMIDE POLYMER FOR DRUG DELIVERY APPLICATIONS.**MANJUNATHA M¹., JAGADISH R.L¹., *GOWDA D.V.² AND MOHAMMED S. KHAN²**¹department of studies in polymer science, mysore university, mandya.² department of pharmaceutics, j s s college of pharmacy, jss university, mysore.**Corresponding author*

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ABSTRACT

Polymers are ideal class of materials to cover large application areas due to their light weight, biocompatibility, non-corrosive nature, chemical inertness, low cost and comparable densities with that of human organs. The usage of polymers is increasing day by day due to some of their special features which include higher strength to weight ratio, the ease of processability, low cost, light weight, inertness (in most cases), amenability to get a specific property etc. The present study aims for synthesis of biopolymer which is bio compatible and non toxic and which will envisages a tool for the drug delivery. Polymer is characterized by FTIR and DSC which shows presence of moiety present in required polymer. Acute toxicity testing is done in order to render the polymer acceptable for therapeutic use.

KEYWORDS

Polymer, biodegradable, toxicity, synthesis, poly ester amide.

INTRODUCTION

Polymers are natural or man-made molecules, frequently called macromolecules. They are composed of smaller units, monomers, which have reacted together to give a long chain, rather like a string of beads. In the simplest polymers, the monomers are identical and the polymer is named by prefixing 'Poly' to the name of the monomer from which it is derived.¹ They may be defined as large molecules built up by repeated structural units joined by the covalent bonds.²

Polymers are extremely large molecules are essential for our existence. They are the main constituents of our food (Starch, Protein, etc) our cloths (Poly ester, Nylon, etc.) our house (Wood) and our body (Nucleic acids, Proteins etc). Modern civilization is based on the use of polymers in various sectors like Food, Dress, accommodation, transportation, agriculture, electronics and computers etc., and in many other applications. Polymer Science and technology has made great progress in the last few decades. Our quality of life has become dependent on polymers and on their products and rightly Twenty First century is often called

the “**Plastic age**”. Hence it is essential to study this branch of science to acquire more knowledge regarding their chemistry and properties.³

The development of innovative biopolymer materials has been underway for a number of years, and continues to be an area of interest for many scientists. Fomin (2001)⁴ reported that the end of 20th century saw the worldwide production of synthetic plastics nearly 130 millions/year, while the demand for biodegradable plastics is reported to be growing by 30% each year (Leaversuch 2002)⁵

Bio-degradable polymers are defined as those which are degraded in environment where living cells or micro-organisms are present, such as soil, compost, rivers, lakes, body of human beings and animals through enzymatic or non-enzymatic hydrolysis.⁶ Biodegradation is a complex process including chemical and biological (enzymatic) reactions, which can occur simultaneously.⁷

There are three primary classes of polymer materials which material scientists are currently focusing on. These polymer materials are usually referred to in the general class of plastics by consumers and industry. Their design is often that of a composite, where a polymer matrix (plastic material) forms a dominant phase around a filler material (Canadian Patent #2350112- 2002). The filler is present in order to increase mechanical properties, and decrease material cost.

The second class of polymer materials under consideration is partially degradable. They are designed with the goal of more rapid degradation than that of conventional synthetic plastics. Production of this class of materials typically includes surrounding naturally produced fibers with a conventional (petroleum based) matrix. When disposed of, microorganisms are able to consume the natural macromolecules within the plastic matrix. This leaves a weakened

material, with rough, open edges. Further degradation may then occur.

The final class of polymer materials is currently attracting a great deal of attention from researchers and industry. These plastics are designed to be completely biodegradable. The polymer matrix is derived from natural sources (such as starch or microbially grown polymers), and the fiber reinforcements are produced from common crops such as flax or hemp. Microorganisms are able to consume these materials completely, ultimately leaving carbon dioxide and water as by-products. Materials must meet specific criteria set out by the standards ASTM and ISO in order to be classified as biodegradable.⁸

The most important criteria for designing degradable polymers for biomedical applications are biocompatibility of the polymers and their degradation products. Polymers that are made up of naturally occurring building blocks are preferable materials for biomedical applications because their degradation products are non-toxic and can be metabolized properly by living tissues.^{9,10} Considering the above point of view α -amino acid derived polymers – synthetic analogous of proteins could be one of the most promising candidates.

Conventional Poly (α - amino acid)s like the AB type nylon-2 have been extensively investigated by many investigators, and prove to be relatively less suitable as resorbable biomaterials for many reasons given by Nathan and Kohn.¹¹

This diversity in synthetic routes permits us to manufacture polymers having a wide range of material properties at a reduced cost. The recently reported synthesis and *In vitro* studies of regular poly (ester amide) s (PEAs) based on bis (L-phenyl alanine), α,ω – alkylene diesters and adipic acid underwent biodegradation by the action of specific

enzyme like α -chymotrypsin, and the rate of this enzymatic biodegradation increased with the length of the polymethylene chain of the diol used. A strong spontaneous enzyme immobilization on the surface of solid PEAs had also been observed.

An accelerated biodegradation of biodegradable polymers like polyglycolide and PEAs has been suggested to be able to promptly activate macrophages that would, in turn, produce the require growth factors and other biochemicals, for an accelerated wound healing¹²⁻¹⁴.

In addition, these PEAs may be used as new substrates in enzymology as well as for the study of pharmacological and immunologic activities of α -amino acid derived polymers. This diversity in biomedical applications would certainly require a wide variety of mechanical, physico-chemical, and biochemical properties of polymers. In case of AA-BBPs like regular PEAs, such a wide range of properties could be easily achieved by varying three components in building block of the macromolecular backbone during synthesis; α -amino acid, diol and dicarboxylic acid. This additional advantage would make this class of heterochain biodegradable polymers the prominent candidates for our pursuing of better biomaterials. The study has been designed to synthesize new regular poly (ester amide)s consisting of non-toxic building blocks like hydrophobic α -amino acids, α,ω diols, and aliphatic dicarboxylic acids and to study physico-chemical and biochemical properties of the polymer because they have found important use in biomedical applications with special emphasis on drug delivery.

Amino acid – based (PEA)s occupy an unique position in the large family of monomers used to prepare polymeric materials. The higher molecular weight PEAs promotes hydrophilicity with narrow polydispersity and other chemical modifications, as well as exhibited excellent film forming properties.

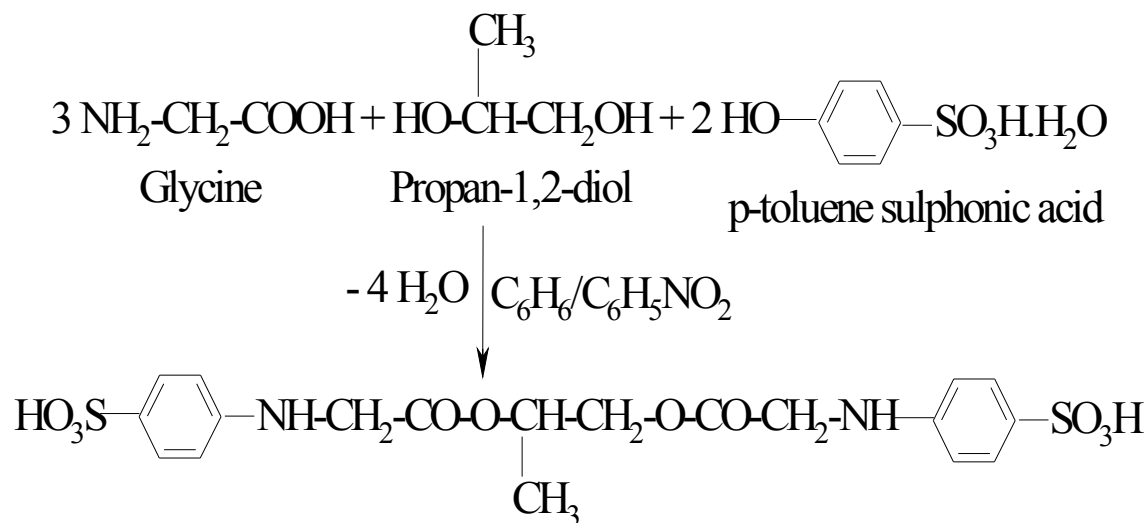
SYNTHESIS AND CHARACTERIZATION OF PEA POLYMER

SYNTHESIS, CHARACTERIZATION OF REGULAR POLY (ESTER AMIDE)S BASED ON BIS (α -AMINO ACID) α - ω ALKYLENE DIESTER, AND ALIPHATIC DICARBOXYLIC ACID

The general scheme of the synthesis of regular PEAs was divided into three major steps and are shown in schemes 1-3: the preparation of di-p-toluene sulfonic acid salts of bis (α -amino acid) α,ω - alkylene diester (1) the preparation of di-p-nitrophenyl ester of dicarboxylic acids(2), and the polymer synthesis of PEAs (3) via solution polycondensation of (1) and (2)

SYNTHESIS OF MONOMER-1:

Glycine (2 mol, 1.5g), propane-1,2-diol (1 mol,0.76ml) were refluxed with a mixture of benzene (20ml) and nitrobenzene (20ml) in a round bottom flask, fitted with water cooled condenser and anhydrous calcium chloride guard-tube. The mixture was refluxed (2 hours), p -toluene sulfonic acid (2 mole, 3.72g) was added and further refluxed (2 hr). The contents of flask were cooled; the precipitate obtained was filtered, washed with benzene/ nitrobenzene mixture and dried.

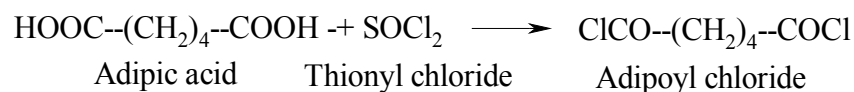
Scheme-1.**Figure 1**

Di-P-toluene sulphonic acids Salt of bis (glycine) α,ω -alkylane diester.

SYNTHESIS OF MONOMER-2***Synthesis of di-p-nitrophenyl ester of Adipic acid.***

Step 1:- Adipoyl chloride was prepared by reacting Adipic acid (1 mole, 4.38g) and thionyl chloride (3 mole, 10.7ml). A clear liquid with a yield of 8ml obtained.

Step 2 :- The di-p-nitrophenyl ester of Adipic acid was prepared by refluxing adipoyl chloride (1 mole, 7.32 ml), pyridine (2 mole, 6.32 ml) in ethyl acetate (20 ml) for 2 hours. P-nitrophenol was added and refluxed. The contents of flask were cooled; the precipitate obtained was filtered, washed with ethyl acetate and dried.

Scheme 2

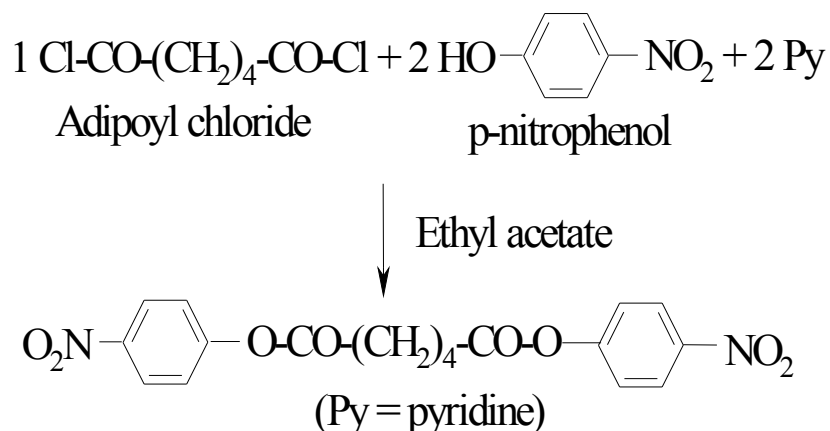
Scheme 3

Figure 2
Synthesis of di-p-nitrophenyl ester of Adipic acid.

SYNTHESIS OF POLY (ESTER AMIDE)¹⁵⁻¹⁷

Monomer (1) (1 mole, 1.3 g), monomer (2) (1 mole, 1 g) and pyridine (2 mole, 0.39 ml) were taken in a round bottom flask containing ethyl acetate (30 ml) and contents were refluxed (3 hr). The contents of flask were cooled and the precipitate was filtered, recrystallised using ethylacetate. The polymer sample designated as PEA was characterized by acid value, thermal analysis,

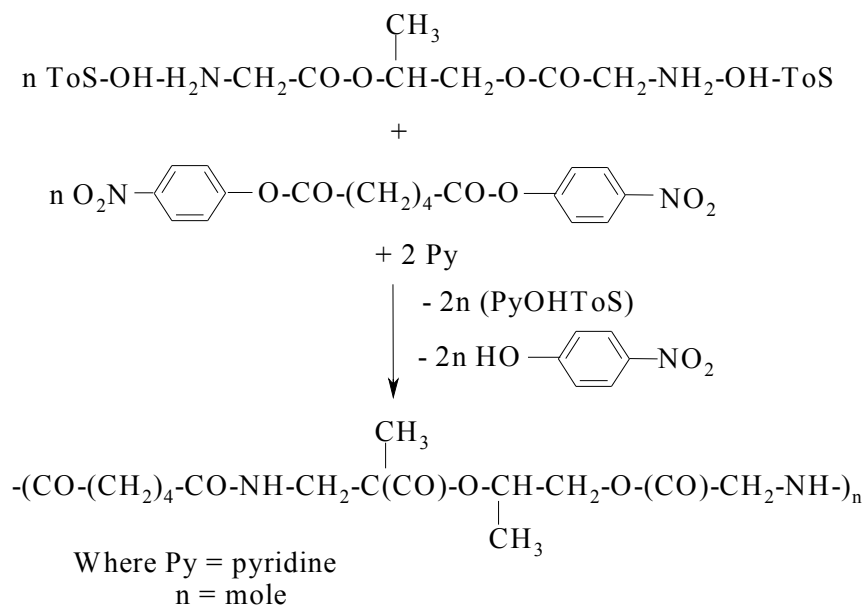
Scheme 4

Figure 3
Poly (Ester amide)s via solution poly condensation of di-p-toluene sulphonic salt, 1 and di-p-nitro phenyl ester 2.

CHARACTERIZATION OF PEA POLYMER**Fourier Transformation Infrared Spectroscopy (FTIR)**

FTIR spectra of the samples were obtained using FTIR spectrophotometer (Shimadzu, FTIR 8400S) by KBr pellet method.

Differential scanning calorimetry:

Differential scanning calorimetry (DSC) was carried out using DSC Q1000 V9.4 calorimeter, coupled to a Shimadzu TA-50 analyzer. Approximately 10 mg of sample was weighed into an aluminium pan which was crimped non-hermetically, and heated at a scanning rate of 10°C/min from 0°C to 300°C under nitrogen purge.

RESULT AND DISCUSSION

Physico-chemical properties and solubility characterization is given in Table 6 and Table 7. The PEA polymer prepared by solution poly condensation is light, slightly semi white powder with high molecular weight, which was measured as a relative value by gel permeation chromatography using tetrahydrofuran as a standard. The softening point is 255°C. The acid value of the polymer sample was found to be 282 mg of KOH/g of the copolymer. Calculated from this value the molar composition of the copolymer was found to be 0.28: 0.12 (MA: PEA). The molar composition of the polymer reveals that PEA content in lower than that in the feed is as follows:

Table 1
Characterization of the copolymer, PEA

Copolymer	PEA
Feed composition (MA: PEA), in mole	0.25: 0.25
Yield (g)	1.14 g
Acid value (mg KOH/g)	282.0
Copolymer-composition (MA:PEA) in moles	0.28:0.12
Softening point °C	255.0
Bulk density, g / cm ³	0.347

Table 2
Solubility characterization of the polymer PEA

Sl.No	Solvent	PEA
1	Chloroform	+
2	Methanol	+
3	Ethanol	+
4	Butanol	+
5	Water	+
6	Ethylacetate	-
7	Hexane	-
8	Toluene	-

The chemical structure of PEA was characterized by FTIR. IR spectrum of PEA recorded using FTIR using KBr pellets shows the characteristic valance oscillations of C=O band at 2929 cm^{-1} indicating the formation of the polymer and presence of acid/anhydride moiety while the ester group signal shown in Figure 4.

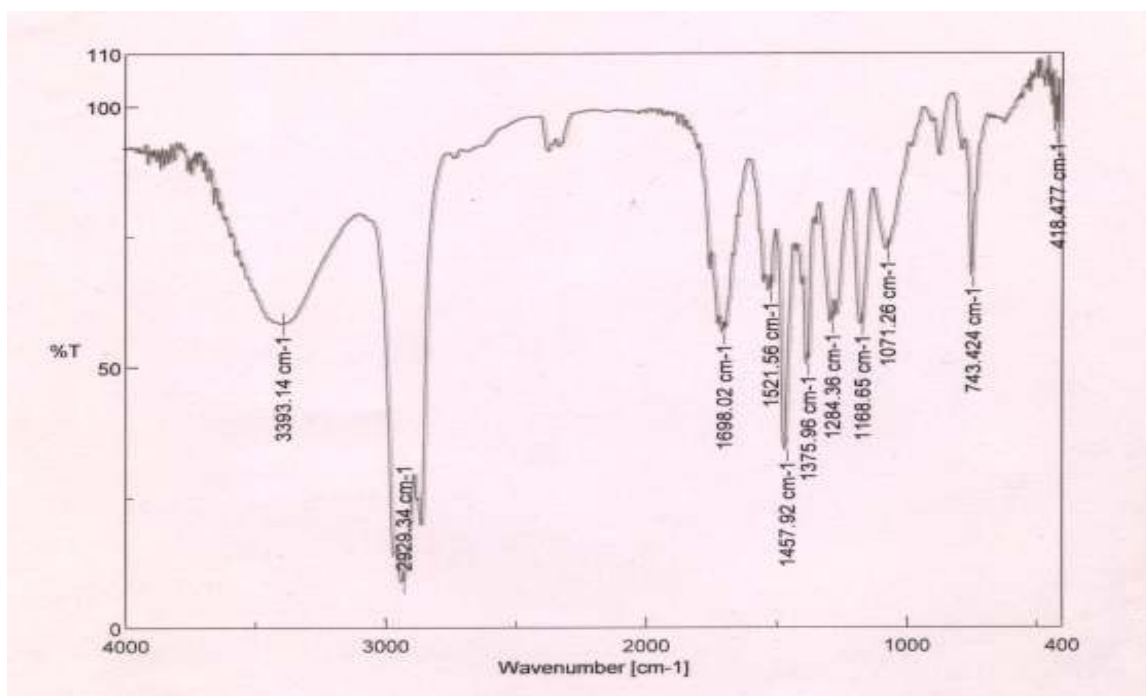


Figure 4.
IR spectrum of poly (ester amide) polymer, PEA.

The structure of synthesized PEA was confirmed by FTIR spectra (Figure-5). The absence of NH_3^+ stretching band at $3100\text{-}2600\text{ cm}^{-1}$ indicates the absence of any free amino acid. At 1595 cm^{-1} - (CO)-O-group absorption band can be seen. A strong band at 1224 cm^{-1} indicates -c-(co)-o-stretching and at 1755 cm^{-1} provides information about the (CO)-of an amide linkage

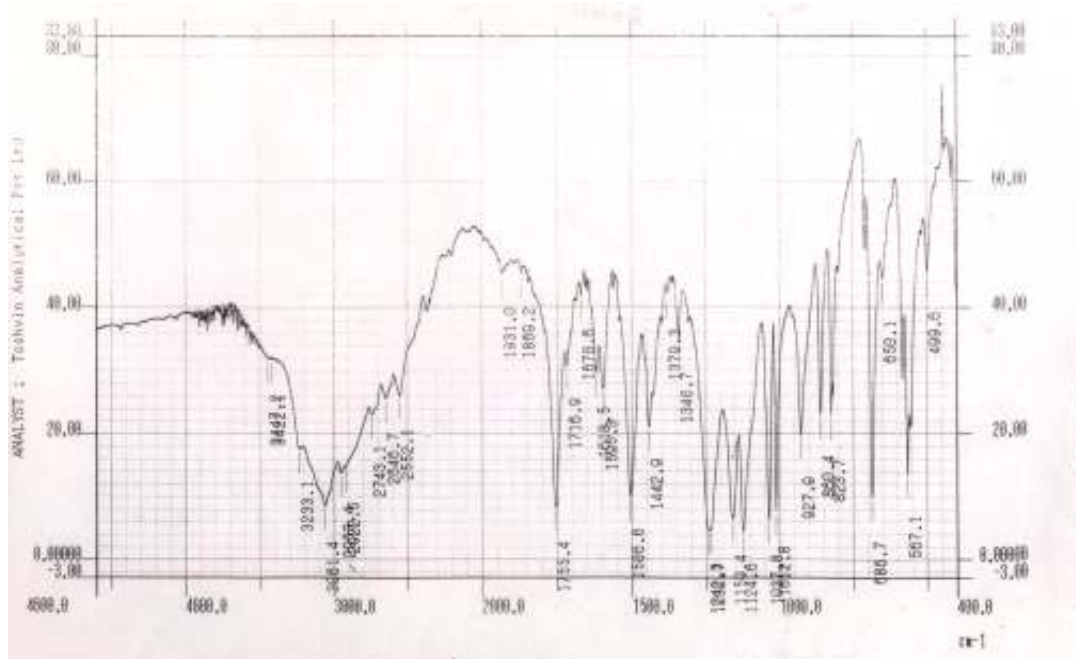


Figure 5
FTIR Spectra of Synthesized PEA

PEA was also characterized by differential scanning calorimetric (DSC) in the temperature range 50-300°C with feed rate temperature of 5°C /minute. The melting point of the polymer sample was found 259°C shown in Figure 6.

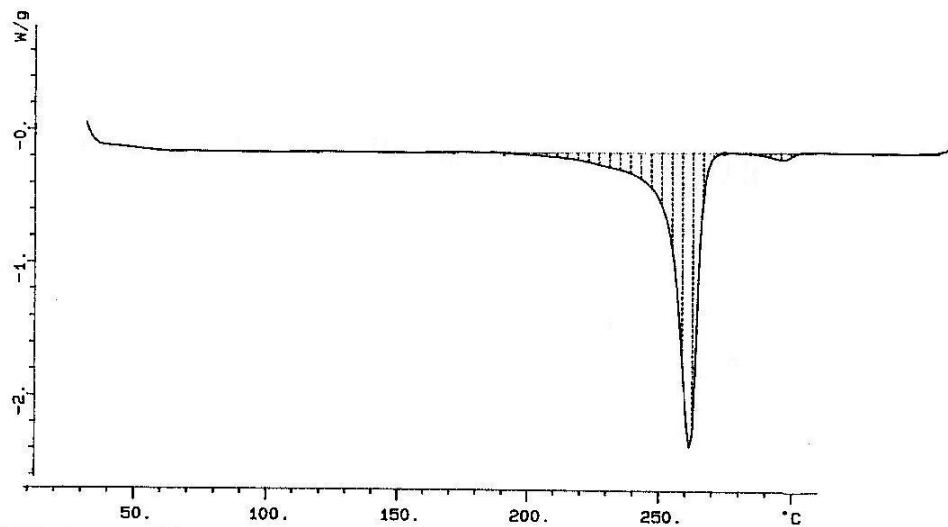


Figure 6
DSC thermogram of PEA

Acute toxicity of the copolymer was evaluated in male and female Sprague-Dawley rats after a single oral dose of 2.00, 200.00 and 400.00 mg/kg of body weight, following the guidelines laid down in Schedule Y of Drugs and Cosmetics Act (1940) by the Drugs Controller of India. The rats were observed for changes in body weight, food consumption, clinical sign and gross necropsy.

ANIMALS

Sprague-Dawley rats male (n=16) weighing were selected for the study shown in Table 3. The animals were housed 2 per cage in polypropylene cages with rice husk as bedding material and the general environmental conditions were strictly controlled in the colony, such as 10% air exhaust in the air conditioning unit, relative humidity of 50±5% temperature 25±3°C and a 14 hr light and 10 hr dark cycle. Animal handling techniques were performed in accordance with good laboratory practice (GLP). Animal house has been registered with Committee for the purpose of control and supervision of experiments on animals, Ministry of Social Justice and Empowerment, Government of India, vide registration No.443 / 01 / a / CPCSEA, dated:25th JULY 2001.

STUDY DESIGN

A. ACCLIMATIZATION: The animals were acclimatized to the laboratory conditions one week before the study and the health status was examined by a veterinarian before the start of the study. Clinical signs and symptoms were recorded a day before the study was started.

B. RANDOMIZATION : Single dose Randomized cross over study was done for each sex, random cage numbers were split into sequential blocks and one block was assigned to each dose level.

C. DOSAGE GROUPS AND DOSE LEVELS :
Animals of both sexes were divided into four groups according to dosage pattern:

1. Control : Vehicle treatment
2. Low dose : 2 mg/kg body weight
3. Mid dose : 200 mg/kg body weight
4. High dose : 400mg/kg body weight

D. ADMINISTRATION OF DRUG/VEHICLE

The animals were administered with the drug/vehicle as a single oral dose on the day of initiation of the study (Table 8)

Table 3
Acute Toxicity Test study Schedule

Group (n=4)	Dose	Male rats	Female rats
Control	0.00 mg/kg	1-4	17-20
Low dose	2.00mg/kg	5-8	21-24
Mid Dose	200.00mg/kg	9-12	25-28
High Dose	400.00mg/kg	13-16	29-32

Numerical values in each group indicated total number of rats viz: 4 for that particular group.

E. STUDY SCHEDULE : Groups of 4 male and 4 female rats were administered PEA polymer

as a single dose in dosages as shown in Table 8.

F. DOSE FORMULATION : The polymer sample was weighed on the day of the study initiation and a suspension was made in freshly prepared 0.2% agar prior to dosing.

Rats were observed for changes in body weight (before start of the treatment, daily and at the end of the study), food consumption (daily and end of study), clinical signs (Day 1 every 1 hr up to 8 hrs and daily twice till the end of the study) and gross necropsy (end of the study). All the animals were sacrificed on the 15th day.

There was no effect on body weight as shown in Table 4, food consumption as shown in Table 5, no major clinical signs were observed during the study period as shown in Table 6 for male rats and in Table 7 for female rats and no abnormalities were detected on necropsy as shown in Table 8. Because no evidence of any toxicity was observed at any dose level, it is concluded that dosage of the PEA polymer up to and inclusive of 400.00mg/kg were well tolerated by the Sprague - Dawley rats.

Table 4.
Summary of Body Weights during Acute Toxicity study

Treatment Dose mg/kg	Average body weight (g)					
	Male rats			Female rats		
	Day 0	Day 7	Day 14	Day 0	Day 7	Day 14
Control (0.00mg/kg)	138.32 ± 14.48	140.33±15.30	232.4 ±2.22	159.14 ±7.12	162.82 ±8.62	196.62 ±6.71
Low dose 2.00mg/kg	117.52 ±6.14	126.62±6.12	224.6 ±2.12	180.00 ±6.24	190.34 ±7.31	206.64 ±7.30
Mid Dose (200.00mg/kg)	105.50 ± 5.42	119.6 ±7.13	140.00 ±6.91	202.32 ±2.45	213.10 ±4.23	228.33 ±5.68
High Dose 400.00mg/kg	118.82 ±3.52	134.6 ±4.21	173.32 ±7.76	117.17 ±4.32	134.65 ±4.21	147.50 ±5.64

Body weight expressed as mean ± SD ; n=4 (number of rats per group)

Table 5
Summary of Food Consumption during Acute Toxicity study

<i>Treatment Dose mg/kg</i>	<i>Food consumption (g)</i>			
	<i>Male rats</i>		<i>Female rats</i>	
	<i>Day 7</i>	<i>Day 14</i>	<i>Day 7</i>	<i>Day 14</i>
Control (0.00mg/kg)	12.12 ± 0.70	12.62 ± 1.02	16.10 ± 0.46	16.64 ± 1.22
Low dose 2.00mg/kg	11.21 ± 1.12	13.12 ± 0.86	16.46 ± 0.72	18.14 ± 0.82
Mid Dose (200.00mg/kg)	10.19 ± 0.66	12.48 ± 1.07	16.07 ± 0.54	16.43 ± 1.07
High Dose 400.00mg/kg	15.73 ± 0.22	17.37 ± 1.00	12.69 ± 0.56	14.02 ± 1.14

Food consumption is expressed as mean ± SD of food consumption/ animal/day; n=4 (number of rats per group)

Table 6
Clinical Sign and Mortality (Male Rats)

<i>Incident hour</i>	<i>Treatment /dose</i>											
	Control (0.00 g/kg)			Low dose (2.00 g/kg)			Mid dose (200.0 g/kg)			High dose (400.0 g/kg)		
Day 1												
	M	C	E	M	C	E	M	C	E	M	C	E
1	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
2	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
3	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
5	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
6	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
7	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
8	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
Day 2												
1	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
2	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
3	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
5	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
6	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
7	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
8	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
9	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
10	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
11	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
12	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
13	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
14	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
Mortality %	0	0	0	0	0	0	0	0	0	0	0	0

M: Mortality,C: Clinical signs,E: EDEMA at Injection site

Table 7
Clinical Signs and Mortality (Female Rats)

Incident hour	Treatment /dose											
	Control (0.00 g/kg)			Low dose (2.00 g/kg)			Mid dose (200.0 g/kg)			High dose (400.0 g/kg)		
Day 1												
	M	C	E	M	C	E	M	C	E	M	C	E
1	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
2	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
3	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
5	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
6	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
7	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
8	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
Day 2												
1	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
2	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
3	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
5	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
6	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
7	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
8	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
9	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
10	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
11	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
12	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
13	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
14	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
Mortality %	0	0	0	0	0	0	0	0	0	0	0	0

M: Mortality,C: Clinical signs,E: EDEMA at Injection site.

Table 8.
Summary of Necropsy findings (Fate: Terminal sacrifice)

Treatment Dose	Findings	Male / Female rats
Control (0.00mg/kg)	No abnormalities detected	4/4
Low Dose (2.00mg/kg)	No abnormalities detected	4/4
Mid Dose (200.00mg/kg)	No abnormalities detected	4/4
High Dose (400.00mg/kg)	No abnormalities detected	4/4

Ethical review: Written approval obtained from local ethical committee of Farooqia College of pharmacy, Mysore, India.

CONCLUSION

The development of innovative biopolymer materials has been underway for a number of years, and continues to be an area of interest for many scientists. Much of attention is focused on synthesis of bio polymers. These biopolymers are formed into the specific end products and used by a consumer. Ideally, the biopolymer will be disposed in a bio waste collection, and later

composted. This process will ultimately leave behind carbon dioxide and water, which are environmental friendly by-products. The present study shows the synthesis of bio polymer which is bio compatible and nontoxic. PEA polymer synthesized shows no effect on body weight, food consumption, no major clinical signs were observed during the study period and no abnormalities were detected on necroscopy on Sprague - Dawley rats. Because no evidence of any toxicity was observed at any dose level, it is concluded that synthesized polymer is nontoxic and compatible and further PEA polymer can be used for polymeric drug delivery.

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