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Bioactive (CO) - Oligoesters as Efficient Delivery Systems of p-Anisic Acid for Application in Cosmetics

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ABSTRACT

In the present study has been conducted on p-Anisic acid and its application in biological systems. The high-performance liquid chromatography has been used to analyse the effect of p-anisic acid. The principal moment of inertia & thermodynamic functions was calculated by adopting the following procedure of formulae by using spectroscopic data & structural parameters. The studies related to the release of p-anisic acid from both (p-AA-CH2-HP)n oligoester (a) and [(p-AA-CH2-HP)x-co-(HB)y] (co)oligoesters (b) were performed in water solution. Biological comparison of in vitro studies presented that the synthesized (co)oligoesters were found to non-toxic in nature non-toxic and were found to tolerant by the HaCaT cells. Both (homo) and (co)oligoesters showed a positive effect on keratinocyte growth, specifically at moderate concentrations.

Keywords: *Biological system; Oligoesters; Spectroscopy; Non-toxic; HaCaT cells.*

1.0 Introduction

The antioxidants obtained from the natural resources have number of benefits, especially for our healthier lifestyle and general well-being, The benefits includes anti-ageing, anti-inflammatory, anti-carcinogenic, and various anti-microbial properties, which promote a growing use in cosmetic products. The antioxidant activities of natural antioxidants have been largely ascribed to the presence of phenolic content [1,2]. Additionally, antioxidants possess very strong preservative properties and they may prevent lipid oxidation in cosmetic products. Besides, sunlight, air and vehicle pollution, and other environmental factors produce free radicals, which could be neutralized by antioxidants. The use of antioxidants in cosmetics aims to create a barrier that helps protect the skin against free radicals produced by oxidative.

N-heterocyclic compounds are of great importance in the field of medicines, drugs, chemistry, and paint industry. There is immense study conducted has on the biological activity of p-Aisic Acid, 1, 2, 3-Trimethoxi benzene, 3, 4, 5-Trifluoro Benzonitule, 2, 4, 6-Trifluoro Benonitrile, m-Methyl methoxy benzene, 5-chloro-o-Anisidine has been studied, the effect on body system by testing them on rats in lab. Their toxic effects and pharmo-kinetic study and their effects are also studies so for this task. Basu et. al, 2008 [1,7] have studied the angiogenic potential of 3-Nitro-4-hydroxy benzine arsonic acid, which is used in poultry industry. B.P. Singh and R.S. Singh [2,8,9] conducted a detailed study on K-quinones, which is important molecule in blood coagulation. Findale et. al,2006 [3,11-14] have published an article on fungi isolated from packaging materials and is used to make the trichloro anisoles. Miller et al [4, 15-16] administered a total dose of 31.8 mg/kg bw of allyl methoxy benzene on pencanling male mice. Jacob et al [5] have studies the effect of 5-bromo-2-deoxyuridine and other bromonated uracils and pyrimidine derivates in the bacteria e coli. P. mirables etc [17-20]. In the present study a detailed study has been conducted on p-Anisic acid and its application in biological systems. The high performance liquid chromatography has been used to analyse the effect of p-anisic acid.

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2.0 Materials and Methods

2.1 Materials

p-Anisic acid sodium salt (sodium p-anisate, 4-methoxybenzoic acid sodium salt for synthesis, Merck India) was used as procured from market. HPLC grade methanol, chloroform, acetonitrile and 0.03% formic acid in water were purchased from Merck, India. The synthesis procedure for 4-Methoxybenzoyloxymethythylpropiolactone (p-AA-CH2-PL) was done as discussed in the research conducted by various research groups [21-24]. The oligo(3-hydroxy-3-(4-methoxybenzoyloxymethyl) propionate (p-AA-CH2-HP)n oligoesters) and oligo[(3-hydroxy-3-(4-methoxybenzoyloxymethyl)-propionate)-co-(3-hydroxybutyrate)], (p-AA-CH2-HP)x-co-(HB)y] (co)oligoesters were obtained via anionic ring-opening oligomerization of (p-AA-CH2-PL) and via anionic ring-opening (co)oligomerization of _-BL with p-AA-CH2-PL, respectively. The synthesis procedure was performed according to studies conducted by Maksymiak and the research group [25-29]. The resulting (co) oligoesters were purified and characterized by HPLC analysis.

2.2 Method

The principal moment of inertia & thermodynamic functions can be calculated by adopting the following procedure of formulae by using spectroscopic data & structural parameters, [4, 16–18].

$Q = Q_{tr}.Q_{rot}.Q_{vib}$

Energy $E^{\circ} - E_{\circ}^{\circ} = RT^2 \dfrac{dInQ}{dT}$

(c) The free energy function $\left(\dfrac{F^{\circ} - E_{\circ}^{\circ}}{T}\right)$ at one atmospheric pressure is expressed as:

$$\left(\frac{F^{\circ} - E_{\circ}^{\circ}}{T}\right) = -RIn\left(\frac{Q}{N}\right)$$

$$= R\left[\frac{3}{2}InM + 4InT + \frac{1}{2}In\left(I_A I_B I_C\right) - In\sigma_0 + \sum_{i=1}^{3n-6} In\left(1 - e^{-\nu_1 hc/KT}\right)\right]$$

(d) The entropy is given as:

$$S^{\circ}RT\frac{d(InQ)}{dT} + R + RInQ - RInN = \frac{\left(H^{\circ} - E_{\circ}^{\circ}\right)}{T} - \frac{\left(F^{\circ} - E_{\circ}^{\circ}\right)}{T}$$

This gives the entropy for an ideal gas in terms of the partition function Q.

However, in case of those molecules which possess more internal rotational oscillations, it is necessary to apply certain modifications in their partition functions as discussed by various workers [84-90]. To a good approximations, free internal rotation partition function of a molecule with a single rotor is given as:

$$Q_f = \frac{\left(8\pi^2 I_m KT\right)^{1/2}}{h\sigma_i}$$

Where σ_i is the no. of potential minima per revolution, also the symmetry number of the internal and I_m is the reduced moment of inertia of the rotating top [90] expressed as:

$$I_m = A_m - A_{mm} = A_m - \sum_i \left[\frac{\left(\alpha_m^{ir} U_m\right)^2}{m} + \frac{\left(\beta_m^i\right)^2}{I_i}\right]$$

Here $A_m = \sum m_k \left(X_k + Y_k\right)^2$ the top moment of inertia about the rotating bond where m_k is the mass of K^{th} atom.

3.0 Result and Discussions

Propreties of p-Anisic Acid: It is an organic compound having an aromatic smell and is well absorbed by inhalation, oral ingestion and skin contact. It is a very toxic compound and can cause enzyme and nerve damage and also there is a danger of suffocation. The common exposure limit is 0.1 ml/m3 due to its dangerous pollutant properties.

Potential acute Health effects: Slightly dangerous in case of skin and eye contact. It may be combustible at high temperatures and slightly flammable in presence of heat; non-inflammable in presence of shocks. It is explosive in presence of open flames and sports. Various physical properties are discussed as follows:

Physical Property	Result
Physical state and appearance:	Solid (Powder red), white
Odour	Odorless
Taste	Sweet
Molecular weight	152.15 g/mole
pH (0.3 g/l)	3-4
Boiling point	277°C
Sublimation temperature	184°C
Critical temperature	182-185°C
Specific Gravity :	1.385
Vapor Pressure	0.2000 at 25°C

3.1 Solubility in different solvents

Solvent Name	Solubility
diethyl ether	Soluble
Cold water	Very slightly soluble
Alcohol/chloroform/ethyl acetate	Freely soluble
Boiling water	More soluble

3.2 Characterization of p-anisic acid using HPLC analysis

Qualitative and quantitative analyses by high-performance liquid chromatography were conducted to study the effect of p-anisic acid. These activities and programmes were performed at Department of Bio-chemistry, medical college, Department of toxicology, C.C.S. University, Meerut and different labs of NGO's with their great country. The literature used for methods are taken from IDR, SM Medical University Library, NGO's library, OSH net library and PUSA Institute and NISCAIR. The mobile phase consisted of 0.3% formic acid in water and acetonitrile. Table 1 shows the solvent gradient used for separation. The flow rate was set at 1 mL/min. The evaluation was performed using diode array detector (DAD) at 254 nm. The samples were analyzed in triplicate. The standard curve of peak area versus acid concentration was constructed over the range from 0.03 to 140 kg/ml and subjected to linear regession analysis (R^2=0.9223). The calibration curve used for HPLC measurements is present in figure 1.

Table 1: It Shows the Solvent Gradient used for Separation in the Study

Time (min)	A (%)	B(%)
0	70	20
5	70	20
10	55	35
20	50	60
25	45	55
30	42	53
35	40	50
40	55	65
45	60	50
50	75	35

Solvent gradient used for high performance liquid chromotography (HPLC) analysis And the necessary conditions for instability of the compound are:

Vapor density: 1.385 g/cm3, Conditions of Instability: Excess heat, incompatible materials dust generation. It is very ractine with oxidising agents. pka dissociation constant: 4.47, Henry's Law constant = 6.41E.09 atm-m3/mole, Atmospheric OH Rate Constant = 9.31cm3/molecule-sec.

Figure 1: Standard Curve of Peak Area versus Acid Concentration

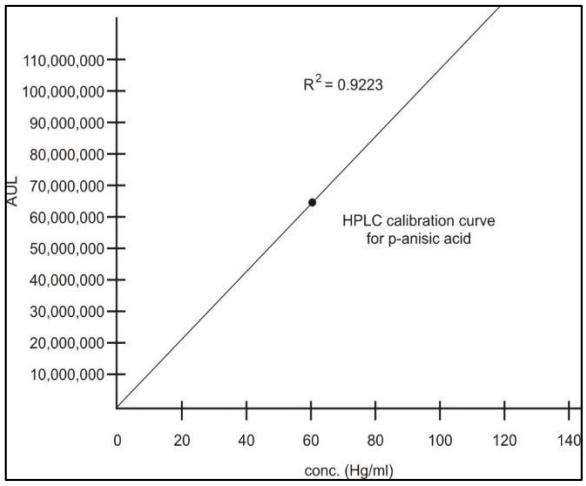


Table 2: Thermodynamic Function of p–Anisic Acid (in cal/ mole *K*)

Temp (*K*)	Enthalpy	Free energy (–)	Entropy	Heat capacity
100	13.15	51.67	63.31	15.61
200	16.38	59.85	68.05	18.75
273.15	19.16	64.65	74.58	21.19
298.15	21.03	67.35	78.29	23.88
300	21.39	68.98	80.68	27.25
400	23.01	74.64	92.93	31.15
500	25.91	78.21	109.26	37.62
600	28.65	82.34	120.15	40.31
700	31.42	87.55	128.19	45.56
800	34.85	94.83	136.41	56.57
900	36.52	97.25	144.76	58.21
1000	41.61	104.66	152.95	60.53
1100	45.37	111.58	166.12	63.93
1200	48.75	116.46	170.28	69.66
1300	51.99	120.75	175.89	75.44
1400	54.61	124.36	179.66	78.88
1500	56.32	126.13	183.85	83.56

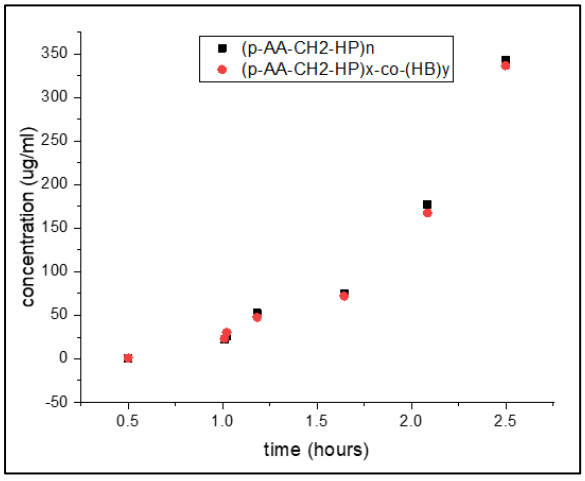
Assessment of Cytocompatibility of (Homo) and (Co)oligoesters Containing the p-Anisic Acid Moiety SRB (Sulforhodamine B) Cell Proliferation Assay.

The human keratinocyte HaCaT cell line (nontumorigenic, spontaneously immortalized cells) were procured from AIIMS Delhi. Cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM), Sigma-Aldrich, India containing 10% fetal bovine serum (PAN Biotech), 100 U/mL penicillin, 100 µg/mL streptomycin, and 20 mM HEPES (pH 7.3; Sigma-Aldrich) Cell cultures were incubated at 37 °C in a humidified atmosphere with 5% CO2. The synthesized (co)oligoesters (samples 1–2) and unconjugated p-anisic acid were dissolved in dimethyl sulfoxide (DMSO) to obtain initial stock solutions. Experimental solutions were made by combining stock solutions with a complete culture medium, and sterile filtered. The final concentration range of the studied compounds was 1–100 µg/mL. DMSO concentration in every culture medium (including control) was adjusted to 0.2%. As a positive control, treatment with 5% DMSO in the culture medium was applied.

Comparative Studies of the Release of p-Anisic Acid from (p-AA-CH_2-HP)$_n$ Oligoester and [(p-AA-CH_2-HP)$_x$-co-(HB)$_y$] (Co)oligoesters.

The studies related to the realease of p-anisic acid from both (p-AA-CH_2-HP)$_n$ oligoester (a) and [(p-AA-CH_2-HP)$_x$-co-(HB)$_y$] (co)oligoesters (b) were performed in water solution at 307 K for the time span of 14 days.

Figure 2: Comparative Release Profiles of p-anisic Acid from (p-AA-CH2-HP)n homo(oligoester) (a) and [(p-AA-CH2-HP)x-co-(HB)y] (co) oligoesters



To analyze the amount and profile of the p-anisic acid release from [(p-AA-CH_2-HP)$_x$-co-(HB)$_y$] copolymers, the mediums collected after a specific period of degradation of (co)oligoesters were analysed by high-performance liquid chromate graphy (HPLC) equipped with a DAD detector. The results of HPLC analysis, including the presence of p-anisic acid and calculated based on the calibration curve of the amount of acid released from the studied (co)oligoesters over time, and are depicted in the Figure 2.

The quantity of p-AA released from (p-AA-CH2-HP)n oligoester (a) and [(p-AA-CH2-HP)x-co-(HB)y] (co)oligoesters (b) was analyzed for 14 days. Initially, a slight high concentration release rate was observed, but after 3 days, the p-AA depicted a relatively slow release rate. From the p-AA release profile, it was clear that about 50% of the bioactive compound used in the study was released from the carrier in the first 3 days in the case of [(p-AA-CH2-HP)x-co-(HB)y] and, in the case of (p-AA-CH2-HP)n, it was high about more than 75%.

4.0 Conclusion

With the objective to develop (p-AA-CH_2-HP)$_n$ and [(p-AA-CH_2-HP)$_x$-co-(HB)$_y$] (co)oligoesters and to find their application in the area of biomaterials, chiefly in cosmetology, comprehensive in vitro cytotoxicity tests and hydrolytic degradation were performed under laboratory condition [30]. Biological comparioson of in vitro studies presented that the synthesized (co)oligoesters were found to non-toxic in nature non-toxic and were found to tolerant by the HaCaT cells. Both (homo) and (co)oligoesters showed a positive effect on keratinocyte growth, specifically at moderate concentrations.

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