Journal of Analytical and Applied Pyrolysis 117 (2016) 17–24

Contents lists available at ScienceDirect

Journal of Analytical and Applied Pyrolysis

journal homepage: www.elsevier.com/locate/jaap

Thermal and spectroscopic characterization, antioxidant evaluation and pyrolysis of losartan with some bivalent metals

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ARTICLE INFO

Article history:
Received 17 November 2015
Received in revised form
26 December 2015
Accepted 29 December 2015
Available online 2 January 2016

Keywords:
Bivalent metals
Losartan
Evolved gas

ABSTRACT

Solid state M-Los compounds, where M stands for bivalent Mn, Fe, Co, Ni, Cu or Zn and Los is losartan. The materials were characterized by Fourier transform infrared spectroscopy (FTIR), simultaneous termogravimetry–differential scanning calorimetry (TG–DSC), simultaneous termogravimetry–differential scanning calorimetry coupled with Fourier transform infrared spectroscopy (TG/DSC–FTIR) and evaluating antioxidant activity with DPPH. The results can be to inform the thermal behaviour, hydration, stoichiometric relationship, metal-ligand interaction, antioxidant capacity and released gases during of the thermal decomposition of compounds. The thermal behavior of the compound showed similar thermal behavior in air atmosphere and nitrogen atmosphere. The gaseous products released under dry air and nitrogen atmospheres were CO, CO_2, NH_3, CH_3NH_2, NO and H_2O, CO, NH_3, CH_3NH_2, HCN, respectively. The DPPH test indicated that the scavenging free radicals from $MnLos_2{\cdot}4H_2O$ and HLos were c.a. 20% higher than the others compounds. These results indicate $MnLos_2{\cdot}4H_2O$ to others investigations as toxicological and pharmacological.

1. Introduction

Various applications have been reported in the literature about association of drugs with organic and inorganic compounds. The studies and development of news drugs are important to new treatment of diseases and production of cheaper drugs [1].

The potassium losartan (Los) (Potassium salt of 2-butyl-4-chloro-1-{[2'-(1*H*-tetrazol-5-yl)biphenyl-4-yl]methyl}-1*H*-imidazol-5-yl)methanol) is a relatively cheap antihypertensive drug and it has free distribution in Brazil, according with Ordinance 971 of May 15, 2012 [2]. Although Los is effective in the treatment of hypertension, it has low oral bioavailability and short half-life (high clearance).

Studies of the association of phenol with Los showed that the compound Los/phenol have antioxidant activity 30% increase, when compared with Los alone. The Los/chlorhexidine showed greater antimicrobial activity against *Enterococcus faecalis* than the chlorhexidine, this association and others, as Los/chitosan/guar gum were also studied as drug-delivery systems [3–5].

Los contains functional groups capable to bind a metal ion, forming stable complexes. Pharmacological point of view, part of the effect of medications could be connected with complexation of metal ions and changes in homeostasis, this evaluation can be carried out by free radical scavenging activity by 1,1-diphenyl–picrylhydrazyl (DPPH) [1,6]. The preparation and investigation of several metal complexes with Los and Los alone have also been investigated using thermoanalytical techniques, X-ray diffractometry, optical and infrared spectroscopy, elemental analysis and biological or pharmaceutical activity [3–8]. The published papers are concerned with elucidating of the possible structure polymorphic forms of Los [7], Los-Cu(II) complexes used for controlled drug release [8], complexes $[Cu(Los)_2(H_2O)_3]_2$ has displayed a moderately superoxidedismutase activity, as deleterious agent when tested on the tumoral osteoblasts (UMR106) [6] and positronium formation in solid transition of Mn, Fe, Co, Ni, Zn with Los [9].

The literature does not report anything about thermoanalytical studies under conditions of pyrolysis of losartan with Mn, Fe, Co, Ni, Cu and Zn ions. Moreover, evolved gas analysis (EGA) allows for a greater understanding of the mechanisms of pyrolysis because these techniques are fast and highly sensitive in detecting organic volatile matter [10].

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http://dx.doi.org/10.1016/j.jaap.2015.12.023
0165-2370/

The aim of the current work was to prepare, characterize and evaluating antioxidant activity the association between losartan and the metal ion Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) to news applications. The compounds were investigated by means of infrared spectroscopy, X-ray powder diffractometry, simultaneous thermogravimetry and differential scanning calorimetry (TG–DSC), simultaneous thermogravimetry and differential scanning calorimetry coupled with infrared spectroscopy (TG–DSC coupled FTIR) and other methods of analysis.

2. Experimental

2.1. Reagents

Potassium losartan (Los) was obtained from Pharmanostra Company, and it was used as received. The metal ion were used from the chlorides ($MnCl_2{\cdot}4H_2O$/Isofar, $NiCl_2{\cdot}6H_2O$/Vetec, $CoCl_2{\cdot}6H_2O$/Vetec, $CuCl_2$/Vetec) and sulfates ($Zn(SO_4)_2{\cdot}7H_2O$/Vetec, $Fe(SO_4)_2{\cdot}7H_2O$/Synth), they were used as received.

2.2. Synthesis

The losartan acid (H-Los) was obtained by addition of hydrochloric acid (HCl 0.5 mol L^{-1}) in Los solution until pH 1.0. The precipitate formed was washed with distilled water until the chloride ions were eliminated, filtered through on Whatman n° 42 filter paper, dried and kept in a desiccator over anhydrous calcium chloride.

The metal compounds in solid state were prepared with continuous stirring by slowly adding a solution of Los to the respective metal chloride (Mn(II), Co(II) Ni(II) and CuII) or sulfate (Fe(II) and Zn(II)) solutions. The precipitates were washed with distilled water until the chloride or sulfate ions were eliminated, filtered through on Whatman n° 42 filter paper, dried and kept in a desiccator over anhydrous calcium chloride.

2.3. Characterization methods

The attenuate total reflectance infrared spectra for H-Los, Los and for its metal compounds were run on a Spectrum 100 FTIR spectrophotometer PerkinElmer, using ATR accessory diamond/ZnSe window. The FTIR spectra were record with 16 scans per spectrum at resolution of 4 cm^{-1}.

Simultaneous TG–DSC curves were obtained using a TG–DSC 1 STARe system, from Mettler Toledo. The purge gases were dry nitrogen and air with flow of 60 mL min^{-1}. A heating hate of 293 K min^{-1} was adopted, with samples weighing about 7 mg. Alumina crucibles were used for recording the TG–DSC curves.

Carbon and hydrogen contents were determined by microanalytical procedures, with a CHN Elemental Analyzer from PerkinElmer, model 2400 and by calculations based on the mass losses observed in the TG curves, since the loss of hydration water and the ligand during thermal decomposition occurs with the formation of the respective oxides, as the final residue has known stoichiometry [1].

The EGA (TG-FTIR) experiments were perfomed using thermogravimetric analyzer (TG–DSC 1) coupled to a FTIR spectrophotometer Nicolet, with a gas cell and DTGS KBr detector. The furnace and the heated gas cell (523 K) were coupled through a heated (T = 498 K) 120 cm stainless steel line transfer with diameter of 3 mm. The compounds were analyzed under the same conditions of simultaneous TG–DSC, using mass c.a.10 mg of samples.

2.4. Determination of the reducing activity of the stable radical 1,1-diphenyl –picrylhydrazyl (DPPH) [1]

The solution of DPPH in methanol (40 μg L^{-1}) was prepared daily; 1.0 mL of this solution was mixed with 2.5 mL of methanolic solutions of H-Los, Los and metal-ligand at different concentrations (50.0, 100.0 and 150.0 μg L^{-1}). After 30 min with continuous stirring at room temperature, the absorbance was recorded at 515 nm on a UV–vis spectrophotometer (Bel Photonics 2000 UV). The absorbance lectures were obtained in triplicate.

3. Results and discussion

3.1. TG–DSC

The thermal stability of anhydrous compounds and final temperature, in both atmospheres, occurs between 453 and 493 K and 923–1073 K, respectively. The thermal stability of H-Los, M-Los (M = Mn, Cu, Fe, Co, Ni, Cu or Zn) and Los were compared and Los showed higher thermal stability due to strong interaction between potassium ion and Los anion. The final residues, in air atmospheres, were Mn_3O_4, Fe_2O_3, Co_3O_4, NiO, CuO e ZnO to respectively metal compounds and H-Los and K-Los were not obtained residues. The volatilization of potassium (Los) probably occurs as chloride, suggesting reaction of chloro of the ligand with this metal ion during the thermal decomposition. The qualitative test with silver nitrate and mass values of TG curve of Los allow suggest the formation of KCl as residue at 951 K (Δm_{TG} = 84.46%; $\Delta m_{calcd.}$ = 83.83%). DSC curve of Los was observed a endothermic peak at 1043 K due to KCl fusion. The exothermic peaks at 987 K and 1129 K were due to oxidation of gases products evaporated, see Table 2 and Fig. 1.

In nitrogen atmosphere, the stable residues could not be formed up to 1273 K due to presence of carbonaceous residues.

4. Air atmosphere

The determination of Los purity was based on the assumption that an impurity will depress the melting point of a pure material (T_o) for which melting was characterized by a melting point (T_f) and an enthalpy of fusion ($\Delta H_{fus.}$). The effect of an impurity on T_o of the Los was determined by the DSC method based on the Van't Hoff equation [1,11]. The obtained DSC curve exhibits an endothermic event corresponding to the Los melting point at

Table 1
Analytical and thermoanalytical (TG*) data for $M(Los)_2{\cdot}nH_2O$ compounds.

Compounds	M (oxide)/ %		Los (Lost)/ %		Water/ %		C/ %			N/ %			H/ %			Final Residue
	Calcd	TG	Calcd.	TG	Calcd.	TG	Calcd.	EA	TG	Calcd.	EA	TG	Calcd.	EA	TG	
$Mn(Los)_2{\cdot}4H_2O$	7.86	7.93	84.72	84.73	7.42	7.35	54.44	54.25	54.22	17.31	17.15	17.28	5.40	5.41	5.38	Mn_3O_4
$Fe(Los)_2{\cdot}2.5H_2O$	8.49	8.13	86.74	86.85	4.77	5.02	55.94	55.28	56.17	17.79	17.54	17.60	5.23	5.31	5.25	Fe_2O_3
$Co(Los)_2{\cdot}3H_2O$	8.39	8.30	85.96	85.74	5.65	5.96	55.23	55.85	55.29	17.57	17.82	17.72	5.27	5.07	5.27	CoO
$Ni(Los)_2{\cdot}2.5H_2O$	7.89	8.05	87.36	87.21	4.75	4.74	55.77	55.23	55.68	17.74	17.48	17.51	5.22	5.01	5.20	NiO
$Cu(Los)_2{\cdot}2H_2O$	8.43	7.51	87.75	88.44	3.82	4.05	56.02	55.87	56.02	17.82	17.81	17.82	5.14	5.11	5.13	CuO
$Zn(Los)_2{\cdot}H_2O$	8.79	9.33	89.28	88.78	1.94	1.89	57.00	56.62	56.59	18.13	17.85	17.61	5.00	5.11	4.96	ZnO

M = bivalents metals *TG in air atmosphere, Los = Losartan, n = H_2O number.