The investigation of pro-oxidant: Effect of a new Schiff base and its metal complexes (Cu, Ni, Co, Zn, Mn)

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ABSTRACT

Background: Multifarious biological activities of Schiff base (SB) derivatives are well-known. **Aim:** In this study aimed that investigation of pro-oxidant effect of ([(2-hydroxybenzylidene)-3methylurea]) derivative SB and its metal complexes. **Material and Methods:** Pro-oxidant effect was determined by antioxidant vitamins levels effect against malonyldialdehyde (MDA), which is an indicator of lipid peroxidation in the serum of rats. To this end; 4-6 weekly Wistar albino rats were injected 25 mg/L 2 weeks subcutaneously for 3 days apart by 1 ml injection of a new compound and were then sacrificed 16 days later. Effect of these compounds serum MDA concentration, which is an indicator of lipid peroxidation, serum antioxidant vitamins A, E, C levels were measured with high-performance liquid chromatograph. In the comparison done among a group. **Result:** It was observed that although other serum parameters were altered, groups in comparison with each other in the MDA, vitamins A, E and C concentrations were not statistically changed. **Conclusion:** It may conclude that the compounds tested the administered dose does not cause oxidative stress.

Keywords: Antioxidant vitamins (A, E, C), high-performance liquid chromatograph, malonyldialdehyde, Schiff base

INTRODUCTION

Schiff bases, aldehyde or ketone compound obtained from the reaction with the primary amine condensation products. Schiff base and its metal complexes are interrelated with diverse pharmacological activities; antiviral,[1] antimicrobial and diuretic activity,[2] antineoplastic,[3] antibacterial-catalytic,[4] anti-inflammatory analgesic and antipyretic agent,[5] antiproliferatif,[6] antitumor.[7]

In study of; identified that Schiff base and derivatives against of OH -induced oxidation of DNA were exhibited high performance antioxidant activity.[8]

In a study published in 2013; founded that a Schiff base derivative Cu complexes were exhibited a strong pro-oxidant property.[9]

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MATERIALS AND METHODS

Materials and instrumentation

All solvents were of analytical-grade reagents. The liquid chromatographic system (Shimadzu) consisted of two LC-20AD pumps, aDGU-20A5 degasser, a Sil20A auto sampler, a CTO-10As VP column oven, an SPD-M20A DAD system, and an RF-10AXL Fld system. The two detectors were connected in series.

Animal treatment

Experiments were performed on male Wistar Albino rats weight 150-200 g and 4-6 weekly. They were allowed free access to food and water. Room temperature was maintained at 22 ± 1°C with a 12- hour's light- dark cycle. The animals were randomly divided into seven groups (Control, L, $[Mn(L)_2]$, $[Co(L)_2].H_2O$, $[Zn(L)_2].3H_2O$, $[Cu(L)_2].4H_2O$, $[Ni(L)_2].2.H_2O$ groups, with each group containing 7 rats. The rats were two weeks subcutaneously for three days apart by 1 ml injection as 25 mg/L of compounds.[10] And all animals were anesthetized with ether and scarified on day 16.

Stock solution of the compounds was freshly prepared before each treatment. They were suspending in corn oil at desired concentration after an initial dissolution in 10% DMSO. This concentration of DMSO by itself produced no observable toxic effect. Control received vehicle alone.

Sample collection

All animals were anesthetized with ether and scarified on day 16. Blood was withdrawn from the heart and collected into glass tubes.[10] They were centrifuged at 4.500 rpm for 10 min for determination of serum vitamins and malonyldialdehyde (MDA). The samples were stored at −20°C until assayed.

Analytical methods

All serum biochemical parameters in this study were measured by high-performance liquid chromatograph (HPLC), using previously described methods for vitamins A and vitamin E.[11,12] Vitamin C and MDA, with minor modifications.[13]

Analysis of vitamins A and E

Serum samples taken from the freezer after dissolution process 0.3 ml serum sample on a 1% ethyl alcohol containing 0.3 ml H_2SO_4 proteins were precipitated by addition. The mixture was vortexes then centrifuged 5 min at 2500 rpm. On the samples was added 250 µl of n-hexane. Hexane fat-soluble vitamins in the medium by the addition of hexane were extract was phase. Hexane was added and the tubes were stirred in vortex and then centrifuged again at the end of centrifugation the hexane phase was carefully separated from the glass tube. Stirred by the addition of 250 µl of sample was centrifuged hexane and n-hexane phase and the hexane phase was combined in a glass tube. Extracted with hexane, dried under nitrogen was carefully removed. The residue was dissolved in 100 L of methanol (10) HPLC was analyzed. Vitamin E in the sample at a wavelength of 296 nm and 326 nm vitamin 5 µ inertsil C-18 (15 mm × 4.6 mm) column and acetonitrile methanol:dic hloromethane:chloroform:hexane (60:10:15:10:5) mobile phase at flow rate 1 mL/min analysis[11] was to be recycling 92% for vitamin A, vitamin E was found to be 96%.

Vitamin C and MDA analysis

A volume of 0.3 ml of serum sample taken. its on by adding 0.3 mL of 0.5 M $HClO_4$ was precipitated proteins. This mixture was then vortexes then by adding pure water on the total volume of 1 ml complete. After 15 min the mixture centrifuged (2500 rpm/min) and then 20 µl of samples taken carefully from above supernatants were injected on HPLC.[12] Mobil phase (potassium phosphate and methanol mixed [65:35]), flow rate 1 mL/min analysis. C-18 (15 × 4.6 mm) column. Wavelength of 254 nm.Ascorbic acid and MDA. While vitamin C for the recovery of 95%, MDA 98.8% was found.

Statistical analysis

Results are expressed as mean ± standard deviation. Statistical analysis and comparison between mean values for cytotoxicity were performed by turkey variance analysis (SPSS 10.0 for Windows; SPSS, Inc., Chicago, Illinois, USA).The least significant difference test was used to analyze antioxidant parameters. Level of Statistical significance was set at $P < 0.05$.

RESULTS

All data are presented in Table 1.

Serum MDA and vitamin A, E, C levels were not statistical changed differently among treatment groups.

DISCUSSION

It has been reported that the structure and conformation of ligand have an influence on the redox potential of the central atom in coordination compounds. The changes (i.e., coordination shaper) in metal ions are related to the change of diverse biological function of the compound. The fundamental knowledge of these laws can be used to synthesize more active complexes or contribute to our understanding of biological properties of natural bio coordinative compounds. Our results appear to confirm the explanations activity is affected strongly by the structure of the ligand.[14]

ROS-mediated oxidation of membrane lipids result in the formation of lipid peroxidation of membrane (LPO) product as MDA.[15] MDA (malondialdehyde) is generally considered to be degradation of HYPERLINK "http://en.wikipedia.

Table 1: Serum levels of MDA and vitamins in the rats treated with ligand and its complexes

Compounds (*n*=5)	Vitamin E (mg/L)	Vitamin A (mg/L)	Vitamin C (mg/L)	MDA (mg/L)
Control	1.39±0.08	0.06±0.10	30.014±0.58[a]	0.73±0.08
Ligand (schiff base)	1.77±0.11	0.10±0.025	29.945±0.33	0.72±0.08
$(Cu[L]_2[H_2O]_4)$	127±0.05	0.54±0.09	28.840±0.29	0.69±0.06
$(Co[L]_2[H_2O]_1)$	1.39±0.08	0.56±0.05	29.912±0.53	0.68±0.08
$(Ni[L]_2[H_2O]_2)$	1.52±0.21	0.84±0.09	29.908±0.62	0.70±0.03
$(Mn[L]_2([H_2O])$	1.50±0.35	0.74±0.07	30.050±0.20[a]	0.69±0.03
$(Zn[L]_2[H_2O]_3)$	1.82±0.48	0.70±0.07	29.938±0.65	0.73±0.34

[a]*P*<0.05. MDA: Malonyldialdehyde

org/wiki/Polyunsaturated_fat" \o "Polyunsaturated fat"polyunsaturated lipids.[16] This compound is a reactive HYPERLINK "http://en.wikipedia.org/wiki/Aldehyde" \o "Aldehyde"aldehyde and is one of the many reactive electrophile species that cause toxic stress in cells.[17]

The cellular antioxidant systems can be divided in two major groups; enzymatic and no enzymatic. Some no-enzymatic low-molecular-weight antioxidant compounds, such as ascorbic acid (AsA), a-tocopherol (vitamin E), and carotenoids are consumed and may fall below normal range.

The relative importance of the antioxidant and pro-oxidant activities of antioxidants are an area of current research, but vitamin C, which exerts its effects as a vitamin by oxidizing polypeptides, appears to have a mostly antioxidant action in the human body.[18,19] However, less data is available for other dietary antioxidants, such as vitamin E,[20] or the HYPERLINK "http://en.wikipedia.org/wiki/Polyphenol_antioxidant" \o "Polyphenol antioxidant" polyphenols[21,22] Likewise, the pathogenesis of diseases involving hyper-uremia likely involve uric acid's direct and indirect pro-oxidant properties.

This work carried out in order toinvolvement in ROS (reactive oxygen species) of new ligands and metal complexes. ROS are formed and degraded by all aerobic organisms, leading to either physiological concentrations required for normal cell function or excessive quantities, the state called oxidative stressdue to their high reactivity, ROS are potentially toxic, mutagenic, or carcinogenic.[23]

CONCLUSION

Our findings show that although serum parameters were altered, this changed; groups in comparison with each other in the MDA, vitamins A, E, and C concentrations were not statistically significant. In summary, it may conclude that the compounds tested the administered does not cause oxidative stress.

Declaration of interest

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Conflict of interest

We have no conflict of interest.

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