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Studies on Catalase-Like Activity of Some Tc-99m Radiopharmaceuticals

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Hydrogen peroxide is an ubiquitous metabolite in living systems, produced at increased levels in a variety of pathological situations. Therefore suppressing or at least controlling H_2O_2 production is important. Catalase enzymes can convert hydrogen peroxide into water and dioxygen and a similar role can be played by transition metal ions or some radiopharmaceuticals. (1) TcO_4^-, (2) Tc-99m mercaptoacetyltriglycine (MAG3) and (3) Tc-99m methoxyisobutylisonitrile (MIBI) were each tested for their ability to catalyse the disproportionation of hydrogen peroxide in the presence of the added base imidazole. It was found that (2) and (3) exhibit acceptable catalase-like activity compared to the Tc-99m pertechnetate.

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1. Introduction

Most of the single-photon tomography procedures in nuclear medicine involve Tc-99m source. As diagnostic procedures should permit activity levels not leading to radiation deterministic effects, only stochastic risks have to be considered and this stochastic risk of ionizing radiation for an individual patient cannot be evaluated. However, in the case of a population of patients it is as a prerequisite to determine the absorbed dose in all irradiated tissues or organs to be affected by the diagnostic procedure. The accuracy and precision in reference level determination of irradiation largely contributes to the evaluation of the effects of exposure to small or infrequently repeated amounts of radioactive substances, as currently used in diagnostic imaging procedures, on patients' health. However, these effects are not fully evaluated in the European context [1].

Hydrogen peroxide may cause molecular damage and, over time, cellular dysfunction. It is a byproduct of oxidative metabolism in organisms. This molecular damage will finally accelerate aging and increase the risk of a number of diseases including cancer and diabetes [2]. Catalase transforms hydrogen peroxide (H_2O_2) to water and oxygen. This reaction is a two-electron oxidation/reduction reaction [3].

In the presence of multivalent metal ions some synergy between Tc radioactivity and its redox properties might be expected. There are many metal complexes containing iron, manganese, copper, etc. considering their catalase-like activity but in present work, some radiopharmaceuticals i.e. Tc-99m pertechnetate (Tc:7+), Tc-99m mercaptoacetyltriglycine (MAG3) (Tc:5+) and Tc-99m methoxyisobutylisonitrile (MIBI) (Tc:1+) were used compared to other studies. Therefore we tested the radiopharmaceuticals for their ability to catalyse the disproportionation of hydrogen peroxide.

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2. Experimental

2.1. Materials

Technetium-99m was milked from a $^{99}Mo/^{99m}Tc$ generator (Monrol AS, Istanbul, Turkey) by 0.9% NaCl solution. This generator contains fission molibdenium-99 adsorbed by aluminum oxide (Al_2O_3) in a glass column. Technetium-99m formed by the decay of ^{99}Mo, is a radioactive isotope having a half life of 6.007 h. MIBI kit was purchased as freeze-dried commercial kit containing 1.0 mg tetrakis (2-methoxyisobutylisonitrile) copper(I) tetrafluoroborate (Monrol AS, Istanbul, Turkey).

2.2. Catalase-like activity studies

Volumetric measurements of evolved dioxygen during the reactions of the (1), (2) and (3) with H_2O_2 were carried out as follows. A 50 cm^3 three-necked round-bottom flask containing 0.30 mL radiopharmaceuticals was placed in a water bath (25 °C). One of the necks was connected to a burette and the others were stoppered by a rubber septum. While the solution was stirred, H_2O_2 (1.33 mmol, 0.150 mL) was injected into it through the rubber septum using a microsyringe. Volumes of evolved dioxygen were measured at 1 min time intervals by volumometry. In cases where imidazole (50 mg) was added this was introduced into the reaction vessel before the addition of H_2O_2.

3. Results and discussion

The catalase-like activity of the radiopharmaceuticals to disproportionate H_2O_2 into H_2O and O_2 was examined at 25 °C by volumetric measurements of evolved dioxygen and experiments were repeated several times to ensure consistency of the results. The time course of the O_2 evolution is shown in Fig. 1, Fig. 2 and Fig. 3.

According to the catalase-like activity studies of (1), (2) and (3) showed activity for the catalytic decomposition of H_2O_2 in the presence of added imidazole and the results are summarized in Table. It should be noted that in the absence of the imidazole the radiopharmaceuticals were either inactive or very weak catalysts for disproportionation reaction. On the other hand, the 1*H*-imidazole base itself caused only a very slight disproportionation of H_2O_2. This reaction was greatly enhanced

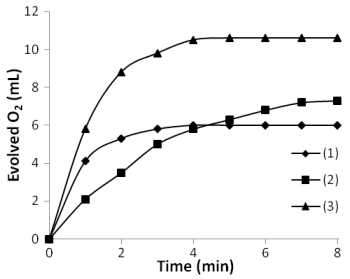

Fig. 1. Time course of dioxygen evolution in the disproportionation of H_2O_2 by the (1), (2), and (3); (radiopharmaceuticals) = 0.30 mL, 370 MBq, (H_2O_2) = 0.15 mL, 298 K.

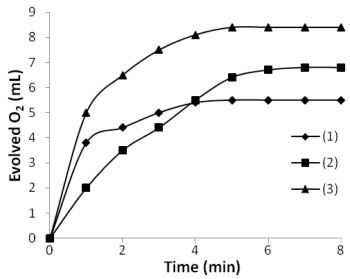

Fig. 2. Time course of dioxygen evolution in the disproportionation of H_2O_2 by the (1), (2), and (3); (radiopharmaceuticals) = 0.30 mL, 740 MBq, (H_2O_2) = 0.15 mL, 298 K.

when the radiopharmaceuticals were included in the reaction mixture with the base. It was found that in case of using MAG3 or MIBI bonded Tc-99m pertechnetate, catalase-like activity was increased significantly where the oxidation state of Tc is (5+) and (1+), respectively. Among radiopharmaceuticals, while the (3) 99mTc-methoxyisobutylisonitrile (MIBI) was the most effective, (1) Tc-99m pertechnetate was the least effective for the catalytic decomposition reaction. The H_2O_2 disproportionation efficiency of the radiopharmaceuticals in the presence 1*H*-imidazole follows the order: $3 > 2 > 1$. In other words the catalytic efficiencies of radiopharmaceuticals in the disproportionate reaction decrease while the oxidation state of the Tc increases.

Continuation of the study, catalase-like activity of the (1), (2) and (3) was performed for their three different doses 370, 740, and 1110 MBq. 0.9% NaCl solution has negative effects on catalytic activity. As the result of this higher radioactivity has less catalytic activity.

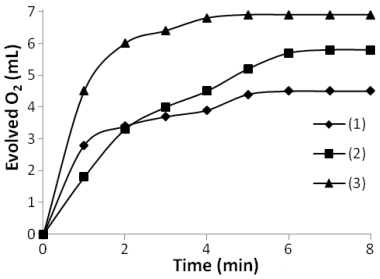

Fig. 3. Time course of dioxygen evolution in the disproportionation of H_2O_2 by the (1), (2), and (3); (radiopharmaceuticals) = 0.30 mL, 1110 MBq, (H_2O_2) = 0.15 mL, 298 K.

TABLE

Time courses of O_2 evolution (mL) from H_2O_2 disproportionated by the radiopharmaceuticals 1-3 with added 1*H*-imidazole (im: 50 mg) at 25 °C [(1): Tc-99m pertechnetate, (2): Tc-99m-MAG3, (3): Tc-99m-MIBI].

Time [min]	1 (370 MBq)	1 (740 MBq)	1 (1110 MBq)	2 (370 MBq)	2 (740 MBq)	2 (1110 MBq)	3 (370 MBq)	3 (740 MBq)	3 (1110 MBq)
1	4.1	3.8	2.8	2.1	2.0	1.8	5.8	5.0	4.5
2	5.3	4.4	3.4	3.5	3.5	3.3	8.8	6.5	6.0
3	5.8	5.0	3.7	5.0	4.4	4.0	9.8	7.5	6.4
4	6.0	5.4	3.9	5.8	5.5	4.5	10.5	8.1	6.8
5		5.5	4.4	6.3	6.4	5.2	10.6	8.4	6.9
6			4.5	6.8	6.7	5.7			
7				7.2	6.8	5.8			
8				7.3					

Catalytic activities of metals and their complexes are usually explained in terms of either their redox potentials or structures [4, 5]. Redox potential of a metal ion has been considered as one of the critical factors in determining the catalytic activity of the catalyst containing the metal ion towards redox reactions, because the reaction appears to involve a change in the oxidation state of the metal ion during the redox steps. The catalytic activity observed for the radiopharmaceuticals is probably due to favorable redox potentials of the technetium.

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