Chemistry of Natural Compounds, Vol. 34, No. 2, 1998

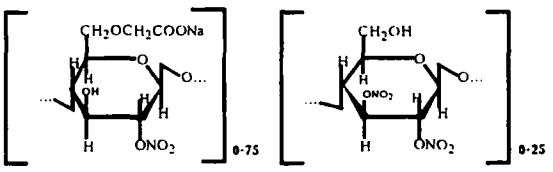
COMPARATIVE STUDY OF THE INFLUENCE OF NITROCEL AND NITROGLYCERIN ON THE *in vitro* BIOSYNTHESIS OF PROTEIN

É. A. Murodov, O. Kh. Saitmuratova, and A. S. Turaev

UDC 541.6.69:615.01

The influence of nitrocel and nitroglycerin on the protein-synthesizing activity of eukaryote nuclei has been studied. Nitrocel has a stronger action on protein synthesis than nitroglycerin.

In medicine, nitro compounds, especially nitroglycerin (NG), are widely used in cardiology with the aim of the prophylaxis and arrest of attacks of stenocardia. In recent years, intensive investigations have been conducted with the aim of creating new drugs possessing improved physicochemical properties. These include the nitro derivative of carboxymethylcellulose — nitrocel (NC) — first obtained by us, which possesses antianginal activity and water solubility. NG is the trinitrate of glycerol, while NC is a nitrate of carboxymethylcellulose having the following structural formula:



All drugs based on known nitro compounds are insoluble in water and therefore have no injectable medicinal forms. The water solubility of NC [1] permits the development of an injectable medicinal form of an antianginal drug, which is extremely necessary in cases of an acute phase of myocardial infarct.

Our task was a comparative study of the influence of NC and NG *in vitro* on the rate of synthesis of protein in isolated eukaryote nuclei.

The influence of NG was investigated with doses of 10, 100, and 200 μg/ml introduced into the incubation medium. It is known from the literature that in *in vitro* systems doses of from 10 to 200 μg/ml are mainly used, while protein preparations, particularly peptides, toxins, and hormones, are used in very small doses. We took three different doses in order to determine the one with the optimum action on the *in vitro* synthesis of protein in cell nuclei.

NC in doses of 10 and 100 μg/ml gradually increased the activity of the nuclei in the synthesis of protein as measured by the inclusion of [^{14}C]lysine into the nuclear protein. Thus, NC in a dose of 10 μg/ml increased the synthesis of protein by 61%, and at 100 μg/ml by 88% in comparison with a control. With a further increase in the dose (200 μg/ml) protein synthesis gradually decreased and amounted to 73% of the norm. Thus, the dose of NC with the greatest effect on protein synthesis is 100 μg/ml.

NG exhibited a weaker action on nuclear protein synthesis than NC. Thus, in a dose of 10 μg/ml the activity of nuclear synthesis increased by 19%; at 100 μg/ml, by 30%; and at 200 μg/ml, by 15% in comparison with a control. The NG dose with the greatest effect was, as for NC, 100 μg/ml. Both substances activated the rate of nuclear synthesis in *in vitro* systems (Table 1).

A. S. Sadykov Institute of Bioorganic Chemistry, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax (371) 162 70 71. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 235-237, March-April, 1998. Original article submitted September 22, 1997.

0009-3130/98/3402-0189$20.00

TABLE 1

Substance	Concentration, μg/ml	Radioactivity, pulses/min/mg of nuclear protein	Rate of protein synthesis %
Control	–	26000	100
Nitrocel	10	42000	161
"	100	49000	188
"	200	45000	173
Nitroglycerin	10	31000	119
	100	34000	130
	200	30000	115

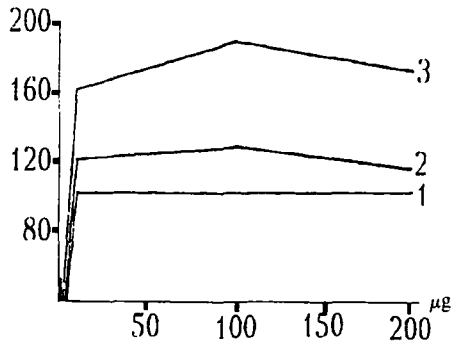


Fig. 1. Influence of various concentrations of NC and NG on the rate of biosynthesis of nuclear proteins after incubation for 60 min: *1*) control; *2*) nitroglycerin; *3*) nitrocel.

It must be mentioned that NC is a polymer. While the molecular mass of NG is 227, that of NC is 5000-7000. The great activity of NC in relation to protein synthesis *in vitro* is due to the macromolecular nature of the drug.

The influence of NC and NG on the protein-synthesizing activity of nuclei is illustrated graphically in Fig. 1.

Both compounds contain $-ONO_2$ groups, which are responsible for their antianginal activity and also for their similar effects on protein synthesis in *in vitro* systems. In our opinion, the similarity of the effects of NC and NG on this process depends on their chemical structure and also on the conformational states of the molecules.

The results that we obtained supplement pharmacological results according to which NC, like NG, not only improves the coronary blood flow of the heart [2, 3] but also intensifies the nuclear synthesis of protein *in vitro*, while its action is more pronounced.

EXPERIMENTAL

Three-day seedlings of a cotton plant of the Tashkent-8 variety were used.

The isolation of the nuclei and the synthesis of protein in the isolated nuclei were conducted by a method described previously [4]. Protein synthesis in the isolated nuclei of the cotton plant seedlings was evaluated from the inclusion of [^{14}C]lysine when samples were incubated at 37°C for 45 min in a rocking water bath, for which we took 0.5 ml of a suspension of nuclei in an incubation mixture containing 0.25 M sucrose, 0.003 M $CaCl_2$, 0.003 M $MgCl_2$, 0.02 M tris-HCl, pH 7, and 10, 100, or 200 μg/ml of NC or NG. The NC preparations studied were synthesized in the Institute of Bioorganic Chemistry of the Academy of Sciences of the Republic of Uzbekistan; the NG was a commercial preparation; 0.05 ml of [^{14}C]lysine with a specific activity of 1 μCurie/mmole (1,000,000 pulses/min) [sic]. After incubation, synthesis was stopped and the labeled nuclear proteins were washed by a known procedure [5]. Protein was determined by Lowry's method [6].

REFERENCES

1. Patent Application No. 1 NDR 9600901, October 16, 1996, Positive Decision [in Russian].

2. A. G. Kurmukov, A. S. Turaev, Sh. Nadzhimutdinov, R. É. Salikhova, and S. S. Rakhimov, Farmakol. Toksikol., No. 3, 55 (1984).
3. É. A. Murodov, A. S. Turaev, O. Kh. Saitmuratova, and A. G. Kurmukov, in: Abstracts of Lectures at the 3rd Conference of the Biochemists of Uzbekistan [in Russian], Tashkent (1996), p. 45.
4. O. Kh. Saitmuratova and O. G. Nemtsov, Dokl. Akad. Nauk RUz, No. 12, 43 (1988).
5. O. Kh. Saitmuratova et al., Neirokhimiya, **6**, No. 3, 360 (1987).
6. O. H. Lowry et al., J. Biol. Chem., **193**, No. 1, 265 (1951).