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The Consumption of Nanocrystalline Cellulose Affects Behavioral Responses *in Vivo*

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INTRODUCTION & AIM

Nanocrystalline cellulose (NCC) has unique physico-chemical properties such as high adsorption capacity and ability to form stable hydrogels. Therefore, NCC is considered an effective substitute for microcrystalline cellulose (food additive E460i). However, the use of NCC in food production is hindered by a lack of knowledge about the risks of its effects on the human body during prolonged consumption with food. It is assumed that the nature of these risks can be associated with special biological effects of fibers (particles) of cellulose in the nanoform and with the residual amounts of chemicals used in its modification. Literary data indicate that experiments to identify the characteristics of the NCC as sources of danger when exposed to the body are contradictory. At the same time, there are no investigations to the present, in which the influence of the NCC on the ability to show neurotropic effects has been studied *in vivo*. Thus, an assessment of the safety of food use of the NCC and the identification of associated risks is an urgent task of food toxicology. The study aimed to assess potential neurotropic properties of NCC using a complex of neurophysiological methods (CRPA, EPM) with the daily consumption of NCC by Wistar rats at doses of 1-100 mg/kg b.w. for 56 days.

METHOD

The NCC ("Nanografi Nanotechnology", Germany, fig. 1-2) was obtained from microcrystalline cellulose (CAS 9004-34-6). The amount of dry substances and moisture in the drug NCC, in accordance with the manufacturer's specification, is 6 and 94%, respectively. Zeta potential: -38 mV.

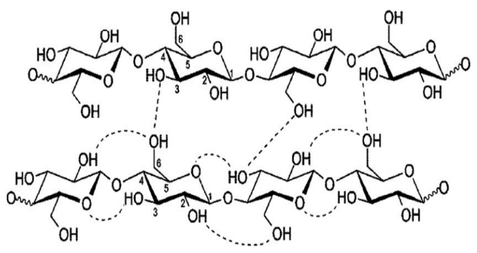

Fig. 1 – Chemical structure of cellulose

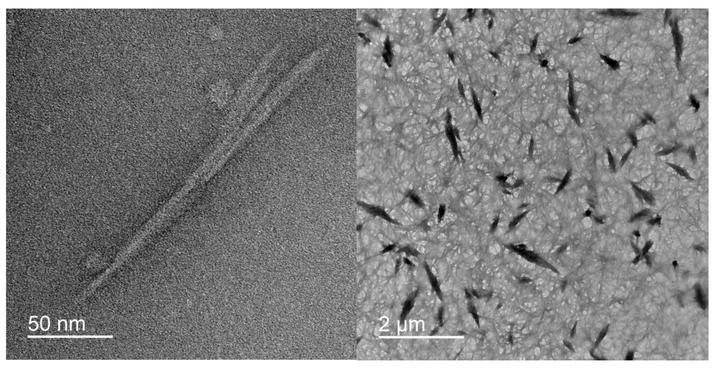

Fig. 2 – TEM ultrastructure of NCC

The procedures for care, maintenance, euthanasia, and experimental procedures were consistent with international guidelines on good laboratory practice. The design (Fig. 3) of the experiment was approved by the Ethics Committee of the Federal Research Centre of Nutrition, Biotechnology, and Food Safety, Russia, Moscow (Protocol No. 7 dated 10/14/2022).

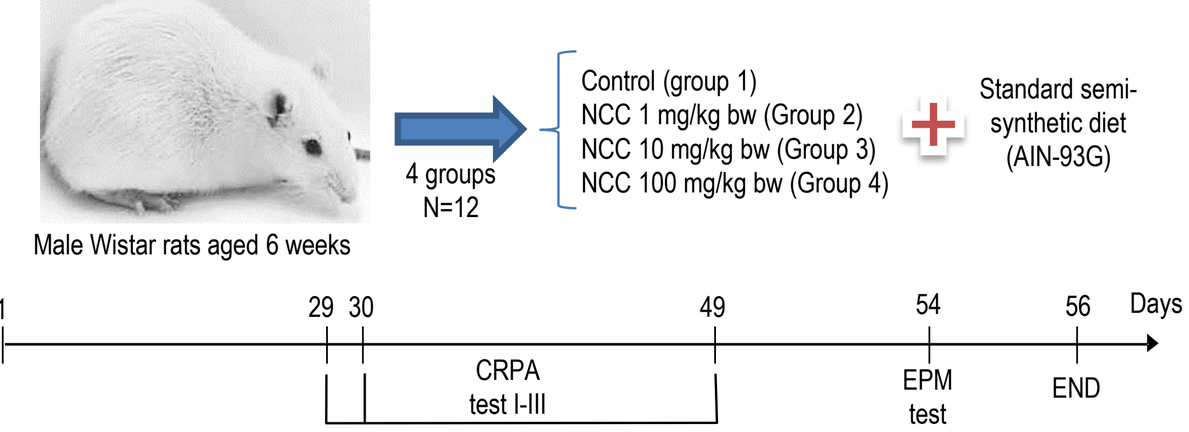

Fig. 3 – Design of the 56-day *in vivo* experiment

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RESULTS & DISCUSSION

In animals that consumed NCC at a dose of 100 mg/ kg b.w., a whole range of significant changes ($p<0.05$) in behavioral reactions (fig. 4a-d) were revealed compared with the control, among which there are signs of anxiety-like behavior. During the first testing in the CRPA (conditioned reflex development), group 4 rats were characterized by a significant decrease in latency time before entering the dark compartment of the facility. As shown by a quantitative analysis of the movement of rats around the EPM maze, there was an almost threefold increase in the ratio of stay in the open (OA, fig. 4b) and closed arms (CA) of the maze compared with the control. A significant decrease in the time spent by rats in the OA (fig. 4c) and an increased time spent in the CA (fig. 4d) were found, along with significant changes in the indicators characterizing the distance traveled in the corresponding arms of the EPM.

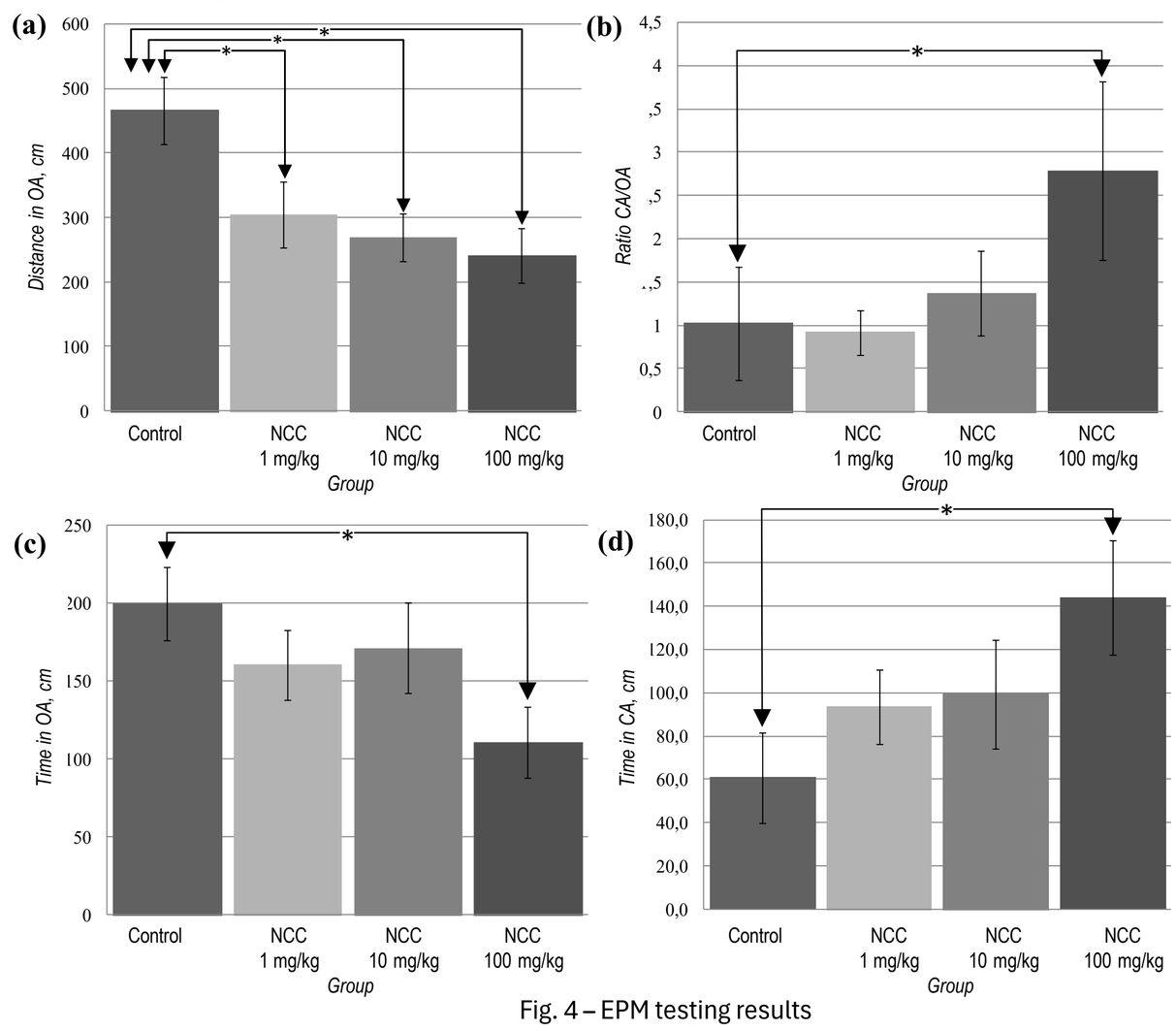

Fig. 4 – EPM testing results

CONCLUSION

Dietary intake of NCC, especially in high doses of 10-100 mg/kg b.w., is accompanied by neurotropic effects in rats. The NOAEL of NCC for a 56-day intake with a diet is, according to the study of behavioral indicators, in any case, less than 1 mg/kg b.w. To understand the mechanisms of the identified effects, studies are required to assess the state of the barrier function of the gastrointestinal tract, microbiocenosis, and the production of short-chain fatty acids.

ACKNOLEDGEMENTS

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