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REVIEW

Enterosorption as a Method for Prolonging Life

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Abstract—Based on an analysis of current literature, this work deals with mechanisms of intoxication and detoxication during the aging process, as well as prospects for applying enterosorption as a detoxication technique for prolonging life.

Enterosorption belongs to scientific field in which Russian researchers are ahead of others. Therefore, the most interesting results have been obtained by them (including researchers from the Commonwealth of Independent States (CIS)). These results generally concern clinics. Currently, information on the possible use of enterosorbents to prolong life has been accumulated. It would be beneficial to review the scientific works published over the past decades in an effort to elucidate the mechanism of enterosorbents' action, and the advantages and limitations of this method as a tool for slowing the aging process.

INTOXICATION AND AGING

Intoxication of the organism always accompanies aging. I.I. Mechnikov long ago considered self-intoxication due to the toxic effects of endogenous and exogenous toxins produced by large intestinal microflora as a main factor causing the disintegration of intertissue relations, which in turn causes aging.

The most effective factors that decelerate aging are hypothermia and a low-calorie diet. It is assumed that these factors decrease the proportion of sideeffects, such as nonenzymatic reactions, which significantly contribute to organism intoxication, resulting in acceleration of aging [1, 2].

Intoxication is closely associated with age-dependent alterations in the genome and cellular metabolism, including the effects of free-radical reactions, when considering the whole organism, generally with all systems of organs and tissues, particularly with the aging of the liver, kidneys, and gastrointestinal tract.

Liver plays an important role in protein, lipid, and carbohydrate metabolism and in holopoiesis, bile secretion, and detoxication; therefore, it significantly affects the maintenance of homeostasis. During aging, a decrease in the hepatocyte number, an increase in the number of polyploid cells, a decrease in the number of mitochondria per cell, a decrease in protein synthesis (particularly in mitochondrial activity), a decrease in respiratory phosphorylation and an increase in oxidative phosphorylation, an extension of the lag-time, and a decrease in inductive (adaptive) protein synthesis occur, accompanied by an earlier onset of cachexia, and probably leading to disorders of the liver system functions, including detoxication [3].

Urinary and biliary excretion of xenobiotic metabolites decreases significantly during aging, which results from the decrease in detoxication intensity. The microsomal oxidative system plays a substantial role in liver detoxication. It was observed that the activities of certain enzymes in the microsomal oxidative system remain unchanged with time, whereas their inductive properties decelerate in parallel with the decrease in response intensity [3].

Kidneys are a vital organ for homeostasis maintenance. The twin organ significantly changes during aging. From the period of embryonal life, the degradation of the nephrons proceeds, characterized by a loss of about 1/3 to 1/2 of the functional units to senility, progressive shunting of the renal blood vessels, an increase in circulatory system resistance (compared with resistance of the total vessel bed), and a decrease in total ATP-ase activity. All these changes lead to an age-related deficit in the main kidney functions due to a decrease in the mean rate of blood flow and glomerular filtration and, furthermore, to a drop in nitrogen excretion. The above-mentioned, combined with an age-specific enhancement of the relative contribution of the humoral compared to the nervous regulation determine the increase in both latent and regenerative periods in the renal response to stress [4].

The gastrointestinal tract has a distinctive function in metabolic relations between the organism and the environment. Digestion, the absorption of nutrients, and coupled processes of discharge occur here. During aging, the cells covering the gastrointestinal epithelium are characterized by a progressive decline in proliferative activity and disturbance of differentiation, which leads to a decrease in the number of enterocytes and main and delomorphous cells, and a reduction in surface and thickness of mucous membrane. With age (from 30-40 years), the volumes of gastrointestinal secretion significantly decrease and, furthermore, the ratios of components and quality of digestive juice are distorted. The age-related involution of the small intestinal mucous membrane is accompanied by a decrease in the oxidation level of enterocytes, a decrease in the number and length of microvilli, and a change in glycocalix. This determines disorders in both membrane digestion and absorption of peptides, lipids, and, to a lesser extent, carbohydrates, and additionally, vitamins and macroelements. It is known that aging is closely connected with a deceleration of the intestinal evacuator function. All the above-mentioned changes in the digestive tract provide the preconditions for quantitative and qualitative shifts in the microflora of the gastrointestinal tube. With the onset of senility, the amount of lactic acid bacteria decreases, whereas the relative portion of putrefactive, pus-producing bacteria, as well as the amount of atypical strains with pathogenic and opportunistic properties, increases against a background of significant growth in the total biomass. Furthermore, changes in the normal relations of cavitary and mucous components of microflora occur [5].

The alimentary canal, kidneys, and liver are the main structures involved in the detoxication processes, but, during aging, even with a slight detoxication insufficiency of these organs, their reactive properties are significantly deteriorated. This is aggravated by age-specific changes in other body systems, mainly in the cardiovascular and neurohumoral systems, which leads to an increase in the frequency of intoxication and to deceleration of the detoxication processes.

THE MECHANISMS OF ENTEROSORBENT ACTIONS

Enterosorbents are the substances that may absorb the components of internal medium after their administration to the lumen of the digestive canal. The mechanisms of enterosorbent action are described in numerous reports. It will suffice to mention the book *Sorbents and Their Clinical Use* [6] and reviews on enterosorption [7-9].

The initial stage of enterosorbent action incorporates physical or chemical sorption of some substances, such as bile acids, cholesterol, indole, scotol, phenols, ammonia, polyamines, and bacterial toxins, in a cavity of alimentary tube [10-12]. This process may be accompanied by an ion exchange or side chemical reactions on the sorbent surface (oxidative reactions, the degradation of peroxyde compounds, transamination, activation of free-radical oxidation, hydrolysis of sugars, lipids, peroxydes, hydroperoxydes, and uric acids) [6, 13-15]. It is necessary to note that the absorbed substances may enter into larger molecular complexes or become elements of the cell surface. In so doing, these side-effects may include the destruction or local increase in the complex or cell concentration on the sorbent surface.

Sorption changes the composition of the internal medium in the lumen of the digestive tube. At the second stage, this leads to a decrease in the concentration of certain substances in the digestive juice absorbed in the lower part of the intestine and to the passive transport of some substances from the body's internal medium through the semipermeable wall of the alimentary canal to its cavity. This also changes the state of the mucous epithelium, modifies the effects of the upper parts of the alimentary canal on its lower parts, modulates the enzymatic reaction of the digestive system to an appropriate stimulation, and transforms the relations between microflora components, as well as between the entire microflora and organism.

The most widespread enterosorbents are pectins, lignins, activated carbons, and highly dispersed forms of silica (silicagels, polysorbogels, and poly sorbs). Pectins and cellulose are the polysaccharides, whereas lignins relate to irregular polymers derived from phenylpropanol. In the literature, these compounds are known as nutritional fibers. They are found in cereals, vegetables, and fruits. Nutritional fibers provide the most physiological natural enterosorbents [8]. There is now a great variety of carbon-containing enterosorbents that differ in structure and chemical composition of the absorbing surface and, therefore, have a different specificity, capacity, and different sorption kinetics [6]. The abundance of raw material and the possibility to readily impart the necessary properties allows one to consider the further development of this type of enterosorbents as very promising. Polysorbs represent one of the extremely strong hydrophylic materials for protein sorption to microorganisms that are easily amenable to chemical modification [16, 17].

DIRECT AND CIRCUMSTANTIAL EVIDENCE ON ENTEROSORPTION INFLUENCE ON LIFESPAN

It is not surprising that enterosorption also has a more profound influence on the organism. Enterosorption decelerates the age-dependent increase in brain sensitivity to some narcotics [1], but it also increases the body's sensitivity to medicamentous therapy [7].

It can be assumed that an enterosorbent in an intestinal lumen acts as a buffer capable of adjusting the variations of some homeostatic characteristics because of the reversibility of the physical sorption of some substances [1].

During enterosorption, the increase of inductive capacities of the microsomal oxidation system in old animals to a level typical of young animals was observed, as well as a decrease of EPR signals corresponding to free radicals and the electron-transport enzymatic systems capable of generating free radicals [1, 18].

Enterosorption determines the normalization of lipid metabolism in old animals, so that its parameters become similar to those in young animals [1, 12, 19]. Analogous results were also shown in clinical practice [20-22]. Use of enterosorbents leads to a decrease in the blood's level of general cholesterol, general lipids, triglycerides, free cholesterol, cholesterol in lipoproteins of low and very low density, and to a normalization of carbohydrate metabolism, liver functions, and rheological blood properties. The aforementioned effects allow one to consider enterosorption as a "pathogenetically conditioned therapy directed to the protection of the organism from excessive amounts of free-radical oxidation products, the normalization of myocardium metabolism, the maintenance of the contractory activity of myocardium, and to the prevention of further damage" [9, 12].

Enterosorption is an effective treatment for chronic renal insufficiency (CRI) [6, 23, 24]. While using the complex therapy CRI, which includes synthetic carbon material as the enterosorbent, along with a normalization of the uremia level and of the characteristics of glomerular filtration, tubular reabsorption, and minute diuresis, only minor changes in the inhibition of the kallicrein-kinin system and in the development of disseminated vascular coagulation syndrome were observed [25].

There is a certain experience connected with enterosorbent use in diabetes mellitus therapy. Thus, enterosorption with carbon sorbents leads to positive effects according to the indices of the compensation rate of carbohydrate metabolism disturbances, blood content of glucose, glycosylation products of lipoprotein atherogenic fractions, and according to the indices of tolerance to physical load [26, 27].

The study that used experimental animals revealed a slight positive effect of fiber carbon enterosorbent on the distribution of intestinal microflora components: a decrease in the proportion of the Gram-negative bacteria population and the growth of lactobacilli and bifidobacteria populations [28].

Enterosorption leads to a deceleration of age-dependent changes, which can be revealed during morphological examination and at the ultrastructural level in liver, myocardium, kidney, cerebral cortex, coronary vessels, and aorta tissue [1].

Enterosorption may be complementary to traditional therapy employed for a variety of diseases, such as viral hepatitis, acute intestinal infection, acute pancreatitis, ischemic heart disease, hyperlipemia, atherosclerosis, diabetes mellitus, bronchial asthma, disorders of the immune system, chronic colites, acute and chronic renal insufficiency, food poisoning, acute leukemia, etc. [7-9], and this list is still growing. These facts testify to the profound corrective effects of enterosorption on the human body, which, in the absence of absolute contraindications, allow one to consider the administration of sorbents to the digestive tract as a reasonable method for the prevention and correction of the effects of aging.

There is direct evidence that shows the effects of enterosorption on the prolonging of life. When carbon sorbent SKN was added to the ration of 20-month-old rats, it resulted in an increase in average life (AL) and maximum life (ML) expectancy of 43.4 and 34.4%, respectively [1]. The 16-month treatment of enterosorption with an active nitrogen-containing carbon employed on 155 Vistar rats led to an AL and ML increase of 35.7 and 36.8%, respectively, and, further, to an increase in spontaneous motor activity and muscle working capacity [29].

The prolonging influence of enterosorption on lifespan is similar to that of a low-calorie diet (LCD). While using enterosorption simultaneously (but not separately) with carbon enterosorbent aerosil and LCD (50% of norm) on male Vistar rats (22 months old), an increase of 56-60% in average life duration was shown [30].

The prolonged administration of enterosorbents does not lead to pathological consequences [13, 14, 31], but the initial action may induce unfavorable results, such as the removal of the mucine layer from the epithelium cells in the digestive tract and a redistribution of enteroflora components. In this case, rather small particles of enterosorbent may induce a high local concentration of pathogenic or opportunistic bacteria and permeate through the epithelium of the alimentary canal. During enterosorption with nutritional fibers and spheric and fibrillar carbon sorbents, an imbalance of minerals, microelements, vitamins, a reinforcement of lipid peroxydation in cellular membranes, and a decrease in protein assimilability may occur. During the administration of dry nutritional fibers, an aggravation of intestinal obstruction may also take place [8]. The influence on the regulation of pancreatic juice secretion was shown for some carbon and silica enterosorbents [32]. Additionally, in some patients without absolute contraindications to enterosorption, an aggravation of the functional state, including a disproportion in the functioning of the immune system and in the ratio of form blood elements, a deterioration of nitrogen metabolism, insignificant abdominal pains, nausea, and vomiting, was observed [7].

Thus, the variety of enterosorbents with different properties permit clinicians to select an appropriate one for correcting the internal body medium, the functional state, and microflora of digestive tract.

CONCLUSION

The analysis carryed out in this work shows that enterosorption is an effective method for prolonging life. Within the field of gerontology, there are two promising lines of enterosorption usage. The first one implies the creation of universal sorbents and regimes of their administration for smoothing out the occasional perturbations in the environment and the body's homeostasis during garmonic aging, and for slowing age-dependent changes evenly distributed over the organs and tissues. The second one is the development of selective enterosorbents oriented to counteract either dominant environmental factors of aging or internal pathology that determines the rate of individual aging.

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