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REVIEW ARTICLE

PREPARATIONS BASED ON HORSE PLACENTA.DIETARY SUPPLEMENT OR DRUG? (MINIREVIEW)

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ABSTRACT

In this mini-literature review, we raised the question of the evidence-based specific effect of horse placenta extract. Questions on the diversity of both its chemical and biological composition are considered. The need for further study of the obtained extracts of horse placenta should depend on the method of their preparation, as this is the only way to exclude the inclusion of certain components of the horse placenta. That will determine the specific factor that has a positive effect on the body.

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INTRODUCTION

The placenta is an important organ that during intrauterine development provides the relationship between the mother and fetus, and also performs respiratory, excretory, trophic, protective, endocrine and immune functions. Currently, a fairly wide range of studies is devoted to studying the possibilities of using placenta extracts obtained by lysis of human placental tissues, sheep, goats, cattle and horses in medicine. Preparations from the placenta have been used for centuries as a traditional medicine, especially in Asian countries. The experience of their use has shown that they contribute to wound healing, liver regeneration, relief of symptoms of menopause and have a significant anti-inflammatory effect. Subsequently, placenta preparations began to be used in clinical practice for the healing of chronic ulcers and burn, wound and radiation injuries of the skin. Such extracts do not contain cells, but possess a wide range of proteins, minerals, amino acids, and steroid hormones (Zheng, 2012). According to various research groups, such extracts have anti-inflammatory, analgesic (Lee, 2011), antioxidant (Togashi *et al*., 2002; Choi, 2014), cyto- and radioprotective (Kawakatsu, 2013), anti-allergic properties (Cole, 2010; Han, 2015; Lee *et al*., 2009), and also stimulate proliferation and repair processes (Cho *et al*., 2008; Ma *et al*., 2012).

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The diverse clinical effects of placenta preparations are a consequence of their complex molecular composition. To date, data on the exact composition of placenta preparations is contained in many publications on biochemistry, molecular biology and pharmacology, as well as in numerous databases of proteins and DNA. The placenta contains more than 4000 different proteins, including growth factors, cytochromes, fibrinolysis factors, energy metabolism enzymes, etc., identified prostaglandins and other neuropeptides, a number of microelements (primarily significant amounts of organic zinc). Most of the research is devoted to the study of the biological properties of extracts obtained from human placenta. So it was shown that placenta extracts enhance the proliferation of fibroblasts and cord blood cells in vitro (Han, 2015; Ma, 2012). The cytoprotective and antioxidant properties of the extracts are associated with protein components; in particular, with alpha-fetoprotein (Togashi *et al*., 2002; Choi, 2014). Model animal studies have shown that the introduction of extracts increases the resistance of animals to oxidative stress (Park, 2010). Placental extracts reduce the concentration of free radicals and proinflammatory cytokines IL-6, TNF, and IL-1, while increasing the formation of progenitor cell colonies and reducing oxidative and radiation damage to cells in vitro (Kawakatsu *et al*., 2013; Park, 2010). Biosafety analysis of extracts of pork placenta revealed the absence of toxic or mutagenic effects on cell cultures and models of adult animals; however, fetotoxicity in animals in early pregnancy has been reported (Mitsui *et al*., 2015). In the clinic, the pronounced positive effects of placental extracts were obtained in the treatment of wounds, non-healing ulcers and burns, while the rate of epithelization was significantly increased, there was a

decrease in leukocyte infiltration and a decrease in pain syndrome (Shukla, 2004). The mechanism of action of placenta extracts during wound healing is explained by an increase in the level of TGFβ in the early phase of regeneration and VEGF in the late phase, increased angiogenesis and increased expression of CD31, as well as the presence of FGF in placental extracts (Park, 2014; Hong *et al*., 2010). Experimental studies of the effect of placenta extracts on the behavior and physical condition of animals showed a decrease in fatigue symptoms and increased resistance to physical activity (Moon, 2014). This was explained by an increase in intracellular calcium, activation of splenocytes and T cells, as well as a decrease in the synthesis of pro-inflammatory cytokines associated with fatigue (IL-6, TNF and IFNγ) (Moon, 2014). Similar results were obtained in preclinical studies (Park *et al*., 2016). Placental extracts have been shown to be highly effective in neurology, supporting the regeneration of nerve tissue in the experimental treatment of nerve damage and facial spasm. The authors explain the effect obtained by increased synthesis of regenerative factors GAP-43 and Cdc2 after exposure to placental extracts (Seo, 2006; Jo, 2013). Placental extracts were effective in the treatment of rheumatoid arthritis (Yurchenko, 2014) and experimental renal failure (Yurchenko, 2013). A certain amount of practical experience with the use of placenta extracts has also been accumulated in veterinary medicine. Here, the extracts were used to stimulate mammogenesis, lactogenesis, and galactopoiesis (Cotor, 2011).

The immunomodulating properties of placental extracts have been shown previously (Fang *et al*., 2007; Georgieva *et al*., 1995; https://patents.google.com/patent/CN103408634A/en). Thus, Chinese researchers isolated and purified several fractions of immunomodulating peptides from a water-soluble extract of cow placenta and characterized there in vitro effect on lymphocyte proliferation (Fang *et al*., 2007). The immunomodulating activity of the extract of pork and horse placenta on mouse lymphocytes was demonstrated (Georgieva, 1995; https://patents.google.com/patent/CN103408634A/en).
t was suggested that peptides with a molecular weight of up to 10 KDa are the main bioactive fraction of the placenta with immunomodulating and antioxidant effects (Hyun *et al*., 2011). For extracts derived from animal placenta, studies of sheep placenta are the earliest and most widely used. In connection with the success of the study of the placenta of sheep, more attention is being paid to studying the possibilities of using for medical purposes extracts from the placenta of other animals (for example, cattle, pigs, etc.). The placenta of horses is currently the least studied. Given the national characteristics and traditions of the peoples of Kazakhstan, where the horse is a traditional source of food and folk remedies, it seems advisable to explore the placenta of horses and scientifically substantiate its healing properties. It should be noted that the use of the placenta of horses does not harm the environment and does not upset the ecological balance, as it relates to natural biowaste.

Conclusion

The presented literature search shows that according to the results of various pharmacological studies of placenta extracts, they are confirmed to be used for immunoregulation, early healing, neurotrophic therapy and hepatoprotection.
However, what exactly from the huge mass of biological substances has a positive effect is still not known. So in the framework of the project No. AP05134106 “Development of biologically active preparations based on horse placenta” we will develop a method for the manufacture of horse placenta extract, and we will also study specific reactions to a specific composition. Since the clinical effects of placenta extracts are a consequence of the complex molecular composition of placental preparations, only a study of the individual components of the obtained extract can answer the question.

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