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Possibilities of using platelet-rich plasma in medicine, cosmetology and veterinary medicine. Review article

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Summary
Platelet rich plasma (PRP) is an autologous preparation obtained from blood. It has an increased number of platelets, and thus a high concentration of growth factors involved in the tissue renewal of the body. Platelet rich plasma is currently widely used in medicine, cosmetology and veterinary medicine. The method of obtaining PRP and an overview of its most common applications is presented below.

Key words: platelet-rich plasma, PRP use, PRP types, platelet-rich plasma effect, production method.

Introduction
Platelet-rich plasma (PRP) - a blood-derived, autologous preparation containing an increased amount of platelets suspended in the plasma. It is obtained from peripheral blood collected from a human being or an animal after centrifugation. It contains numerous growth factors stimulating regenerative processes, so it is used in regenerative therapy of joints and soft tissues as well as in accelerating wound healing processes in animals and humans. It is most often used in the treatment of skeletal muscle injuries, tendons and ligaments, joint injuries, joint diseases, including osteoarthritis, fractures and bone non-union after fractures, inflammation of bones, accelerating the healing of soft tissues, accelerating the process of ulcer healing, as well as wider and wider application in aesthetic and plastic medicine. Platelet-rich plasma is obtained by centrifuging venous blood collected from the patient. Centrifugation causes the separation of morphotic blood elements depending on the weight. Such activity

allows for thickening of platelets (PLT). Platelet alpha-granules contain significant amounts of proteins called platelet-derived growth factors. These proteins play a key role in tissue healing and regeneration processes. The PRP administration method is currently widely used in medicine, cosmetology and veterinary medicine.

Way of action, methods of preparation, distribution of preparations obtained from platelet-rich plasma.

The concentration of platelets in the centrifuged preparation is 2-9 times higher than in the venous blood (about 1000 G/l in relation to 150 - 400 G/l) [1]. The concentration of platelets below twice the concentration does not show the effect on the acceleration of wound healing [1]. Similarly, exceeding the ten-fold concentration also does not tend to improve the results of the treatment [2].

The most important growth factors contained in platelet-rich plasma include: transforming growth factor, platelet-derived growth factor, insulin-like growth factor, epidermal endothelial growth factor, epithelial growth factor and fibroblast growth factor.

Table 1. Growth factors in platelet-rich plasma and their functions [3].

Growth factor	Function
Transforming growth factor - beta 1 (TGF-beta1)	It regulates the metabolism of osteoblasts, causes the development of extracellular matrix.
Fibroblast growth factor (FGF)	It promotes the growth and differentiation of chondrocytes and osteoblasts.
Platelet-derived growth factor (PDGF)	It stimulates the replication of mesenchymal cells and osteoblasts. It is a chemotactic factor for fibroblasts. It accelerates the synthesis of collagen. It has a proangiogenic function.
Epithelial growth factor (EGF)	Chemotactic factor for endothelial cells. It regulates the activity of collagen formation. It accelerates the formation and differentiation of endothelial cells.
Vascular endothelial growth factor (VEGF)	It speeds up the process of creating blood vessels.
Insulin-like growth factor 1 (IGF1)	It is a chemotactic factor for fibroblasts. It promotes differentiation and replication of osteoblasts.
Platelet factor 4 (PF-4)	It is a chemotactic factor for fibroblasts.
Human platelet-derived growth factor (PDGF)	It initiates replication of keratinocytes and fibroblasts.
Hepatocyte growth factor	It favors the formation of blood vessels. Mitogenic factor for endothelial cells.

The production and obtaining of platelet-rich plasma involves taking venous blood from the patient. It is mixed with an anticoagulant (sodium citrate) by inserting into a company test tube, which is placed in the centrifuge. After centrifugation, a blood platelet layer with a small amount of plasma is obtained. These activities last approximately 20 minutes and a product ready for administration to the patient is

obtained. There are several systems for PRP production on the Polish market. The differences between them concern the amount of blood taken (from 10 to 120ml), the number of centrifuges, the degree of compaction of platelets, the volume of the obtained product (from 3 to 30ml) [4].
In some centers, thrombin or calcium chloride is added when the platelet-rich plasma preparation is injected. These substances in contact with PLT cause their activation and immediate ejection of plasma growth factors [5].
In 2014, the classification of platelet-rich plasma by Ehrenfest was established, currently two forms is distinguished: with a high content of leukocytes and with low content of leukocytes. PRP with a large amount of leukocytes is obtained by fast or two-fold centrifugation of the preparation. Then a so-called buffy coat is formed. A single, slower centrifugation results in obtaining of leucoreduced PRP.
Table 2. The types of platelet-rich plasma (PRP) [6].

	Platelet-rich plasma with low leukocyte content (LP-PRP)	Platelet-rich plasma with high leukocyte content (LR-PRP)
Production method	Obtained from plasma	Obtained from a buffy coat
Leukocytes	The minimum number	Present in large quantities
Multiple platelet compaction	1.5 – 3x	5 - 9x

In the light of current studies, the advantage of platelet-rich plasma with a high content of leukocytes in the treatment of tissue damage and its leucoreduced variant cannot be clearly stated. Leukocytes through the secretion of proinflammatory cytokines may adversely affect the healing of wounds. On the other hand, Cieślik-Bielecka et al., showed in their studies the mechanism of accelerated healing of infected wounds under the influence of LR-PRP [7].
The current state of knowledge on the efficacy of treatment with platelet-rich plasma preparations is unsystematized and has a considerable randomness error. Reports are based on case studies, small groups of examined and case reports. They do not have much scientific significance. There is a lack of extensive randomized clinical tests. The situation is further complicated by the fact that there is a large variety of equipment and techniques used to obtain PRP.

The use of platelet-rich plasma in orthopedics and traumatology.

It is used most often in orthopedics and in the treatment of PRP injuries in:
- treatment of tendinopathy,
- treatment of joint degeneration,
- after the injuries of muscles and ligamentary apparatus,
- during arthroscopic surgery,
- in the treatment of delayed bone union or pseudoarthrosis.

Chronic tendinopathies are most often caused due to the accumulation of micro-injuries or tendon overloads overlapping in the course of time. Until the tendon can react to adverse changes by its plasticity and remodel, there is no permanent damage to the collagen fibers and vessels that nourish the tendon. In the situation of prolonged unfavorable burdens of the excessive force, permanent damage to the above-mentioned structures occurs. The tendon defends by the abnormal increase in number of the intercellular matrix. If these remedial options are exhausted, the irreversible degenerative tendinopathy occurs [15].

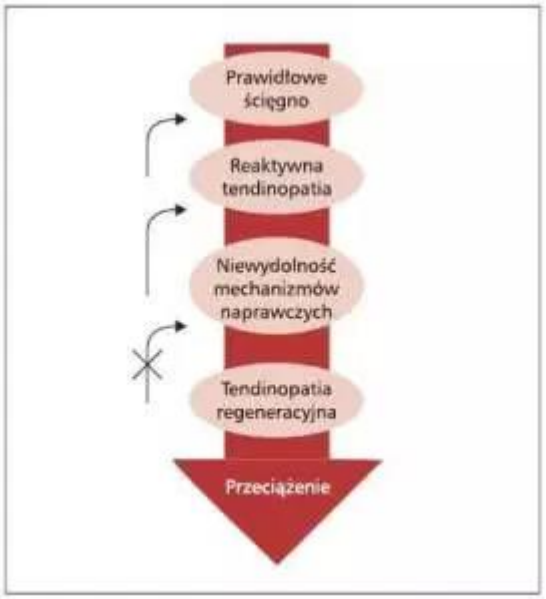

Fig. 1 Pathogenesis of regenerative tendinopathy [28]
The right tendon
Reactive tendinopathy
Failure of repair mechanisms
Regenerative tendinopathy
Overload

The administration of PRP to damaged tendons gives hope for reversing or at least halting degenerative processes, reducing edema of structures and alleviating pain. In the studies described by de Vos, platelet-rich injections were given to patients with Achilles tendon pathology. Patients were divided into two groups. One group was given physiological saline, the other group was given PRP. The results of these studies did not give a definite answer because both groups of examined reported a significant improvement in health [16]. Further studies carried out, among others, by Peerbooms [17] or Krogh [18] brought much better results. Patients in the PRP injected group and in the control group reported improvement in the local condition to the same extent for the first 10-12 weeks, however, in the subsequent months, the patients receiving the platelet-rich plasma experienced a significant improvement. One year after the experiment, 79% of patients reported improvement in health after PRP administration and 49% after the physiological saline injection [17, 18].

Osteoarthritis is now a major diagnostic and therapeutic challenge. Modern man living over 80 years is exposed to the development of severely intensified arthrosis mainly concerning the joints of the lower limbs. In the degenerative process of joints in their lumen, catabolic processes within the chondrocytes have the advantage, which leads to the degeneration of joint cartilage. During this process, inflammatory mediators are released into the lumen of the joint. It is likely that growth factors in platelet-rich plasma beneficially affect the joint's structure, leading to the arrest of arthrosis and even the reversal of some of its effects [19]. Clinical studies concern mainly the knee joint. In the studies of Patel et al. a group of 150 patients divided into three groups was examined. The first group was given physiological saline in place of injury, the second one was injected with PRP, the third group received a double dose of PRP. The results of the study were assessed using pain scale and WOMAC scale (Western Ontario and McMaster Universities Arthritis Index Score).

In the results, a significant improvement in health was obtained in patients who received PRP, both after 3 and 6 months in relation to the patients who received placebo [20].

In the case of treatment of ligamentous injuries with the use of platelet-rich plasma preparations, there is a small number of references in the literature. These relate to the administration of PRP in cases of reconstruction of cruciate ligaments of the knee. There

were no differences in the healing of transplants between treatments with plasma administration and without its injection [21].

Interesting studies were conducted by Kon et al. who administered PRP to the shoulder joints after completing arthroscopy. They obtained a significant analgesic effect both immediately after the treatment and within a month after it - the patients had a reduced need for analgesics [19].

The above reports led to the recognition by International Olympic Committee the administration of platelet-rich plasma as a method for effectively treating chronic tendinopathies, but the effectiveness of this method in the treatment of fresh injuries of muscles and tendons was not recognized.

Application of PRP in aesthetic medicine.

Over the years, aging processes within the skin intensify. Degenerative changes mainly concern the papillary layer of the skin, in which the disappearance of elastic and collagen fibers occurs. Group 1 metalloproteinase, released during exposure to UV radiation or smoking, have a significant influence on this state of affairs. There are two main groups of factors that cause skin aging: extrinsic and intrinsic. Intrinsic factors are conditioned by the type of skin, its phototype and mimicry. They can also depend on the hormonal balance of the body, mainly on the metabolism of growth hormone, estrogen and DHEA. Extrinsic factors include climatic conditions, UV radiation, lifestyle (alcohol, tobacco, stress) [22, 23]. Changes in skin structure concern the whole body, but they are particularly visible in the face and neck area.

The growth factors described above also affect the skin cells, stimulating them to renewal and affecting its good appearance and condition. The preparation for use in aesthetic medicine and cosmetology is obtained in the same way as PRP used in various fields of medicine.

After the injection of plasma into the skin tissue, the activation process of platelets and possibly leukocytes begins (if we give LR-PRP). They eject a chemotactic substance for macrophages that migrate into the connective tissue. Also the following are secreted: growth factor that stimulates the development of mesenchymal cells, a proangiogenic factor affecting the development of blood vessels within the skin, and polypeptides and enzymes that stimulate the activation and differentiation of stem cells. PRP stimulates the production of collagen by activating fibroblasts. The entire range of these processes affects the renewal of superficial and deep skin layers [24].

In aesthetic medicine and cosmetology, three types of treatments are most commonly used: mesotherapy, filling and the so-called mask. The first two treatments consist in injecting the skin on a certain surface or linearly within the wrinkles. The mask consists in applying a paper layer soaked with PRP to the skin area, it is used after laser therapy or after deep peeling and shortens the healing time. The plasma of the concentrations of 2-4 times and a volume of 3 - 4ml are used for the above-mentioned treatments.

Platelet-rich plasma in various areas of medicine.

The first reports on the use of platelet-rich plasma are from 1987, when Ferrari and colleagues used autologous concentrates of platelets and red blood cells during cardiac procedures. This allowed them to reduce the patients' need for blood transfusions [10]. PRP in cardiac surgery was also used to heal wounds after opening the chest and cutting the sternum. It was shown that after the administration of plasma, the wounds healed better and there were significantly fewer infections [11].

In maxillofacial surgery, PRP is often used to accelerate the healing of autologous bone grafts or implants filling the craniofacial osseous defects. At present there are no reports on the beneficial effect of the use of platelet-rich plasma on the rate of graft healing [12].

However, there are reports of faster bone density in the densitometry test within 3 - 6 months of surgery of the jaw and mandible bones, as well as after dental extraction [8]. Administration of PRP reduced pain in the area of the removed tooth and accelerated the healing of soft tissues. Similar effects were obtained by examining the rate of bone healing around dental implants. Platelet-rich plasma is supposed to cause better adhesion of the material to the bone part of the gingiva.
Another area in which the positive effects of platelet-rich plasma are visible is plastic and reconstructive surgery. Good effects of tissue healing and remodeling are achieved, among others, in the treatment of diabetic foot and reconstructed facial soft tissues. Fast graft coverage with fresh skin and better modelling of soft tissues, mainly subcutaneous tissue, were obtained [13].
In Fenning's work, the PRP's effect was described after major gynecological procedures. Prospective studies of subjective pain experience showed a reduction in symptoms when administering platelet-rich plasma to the area operated after haemostasis. The pain lasted shorter and was less severe than in the group in which PRP was not applied [14].

The use of preparations of platelet-rich plasma in veterinary medicine.

Due to the biological similarity of the composition of human blood and mammals, PRP remains of interest to veterinary surgeons. Plasma preparations are used in racing horses affected by tendinopathy and degenerative joint changes. PRP in veterinary medicine is also used in the case of hard-healing wounds, burns and ulcers. Plasma preparations are mainly used to treat horses and dogs [25,26,27].

Summary

Unfortunately, our knowledge about the security of using PRP is still quite limited. It is postulated to avoid using the activator of bovine thrombin for fear of prion infection. Other types of activators are proposed, e.g., collagen of type 1 or synthetic thrombin.
Probably in the following years, due to the great interest in the method, we will witness the development of techniques related to platelet-rich plasma and an increasingly wide range of its applications. As a method of tissue regenerative therapy, plasma preparations give hope for improving the results of treatment of patients with chronic degenerative diseases and chronic wounds or ulcers. It seems that autologous plasma preparations are safe. No side effects were noted. The injection itself does not seem to pose major problems. However, it is now pointed out that PRP should not be administered during pregnancy and lactation, during anticoagulant therapy, in patients with cancer and blood diseases. This type of therapy should also exclude patients with systemic lupus, porphyries, auto-aggressive diseases or metabolic diseases [27wet].
In the near future, the scientific community should focus on developing uniform standards of conduct related to the production and administration of PRP in individual disease entities.

Bibliography:

1. Marx R.E. Platelet-rich plasma: evidence to support its use. J. Oral Maxillofac. Surg. 2004; 62: 489–496.
2. Foster T.E., Puskas B.L., Mandelbaum B.R., Gerhardt M.B., Rodeo S.A. Platelet-rich plasma: from basic science to clinical applications. Am. J. Sports Med. 2009; 37: 2259–2272.
3. Eppley B.L., Woodell J.E., Higgins J. Platelet quantification and growth factor analysis from platelet-rich plasma: implications for wound healing. Plast. Reconstr. Surg. 2004; 114: 1502–1508.

4. Lyras D.N., Kazakos K., Agrogiannis G. i wsp. Experimental study of tendon healing early phase: is IGF-1 expression influenced by platelet rich plasma gel? Orthop. Traumatol. Surg. Res. 2010; 96: 381–387.
5. Harrison S., Vavken P., Kevy S. i wsp. Platelet activation by collagen provides sustained release of anabolic cytokines. Am. J. Sports Med. 2011; 39: 729–734.
6. Castillo T.N., Pouliot M.A., Kim H.J., Dragoo J.L. Comparison of growth factor and platelet concentration from commercial platelet-rich plasma separation systems. Am. J. Sports Med. 2011; 39: 266–271.
7. Cieślik-Bielecka A., Bielecki T., Gaździk T.S. i wsp. Autologous platelets and leukocytes can improve healing of infected high-energy soft tissue injury. Transfus. Apher. Sci. 2009; 41: 9–12.
8. Simonpieri A., Del C.M., Vervelle A. i wsp. Current knowledge and perspectives for the use of platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in oral and maxillofacial surgery part 2: bone graft, implant and reconstructive surgery. Curr. Pharm. Biotechnol. 2012; 13: 1231–1256.
9. Cieślik-Bielecka A., Choukroun J., Odin G., Dohan Ehrenfest D.M. L-PRP/L-PRF in esthetic plastic surgery, regenerative medicine of the skin and chronic wounds. Curr. Pharm. Biotechnol. 2012; 13: 1266–1277.
10. Ferrari M., Zia S., Valbonesi M. i wsp. A new technique for hemodilution, preparation of autologous platelet-rich plasma and intraoperative blood salvage in cardiac surgery. Int. J. Artif. Organs 1987; 10: 47–50.
11. Serraino G.F., Dominijanni A., Jiritano F. I wsp. Platelet-rich plasma inside the sternotomy wound reduces the incidence of sternal wound infections. Int. Wound J. 2013 May 21. doi: 10.1111/iwj. 12087 [submitted to printing].
12. Schaaf H., Streckbein P., Lendeckel S. i wsp. Sinus lift augmentation using autogenous bone grafts and platelet-rich plasma: radiographic results. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 2008; 106: 673–678.
13. McAleer J.P., Kaplan E., Persich G. Efficacy of concentrated autologous platelet-derived growth factors in chronic lower-extremity wounds. J. Am. Podiatr. Med. Assoc. 2006; 96: 482–488.
14. Fanning J., Murrain L., Flora R. i wsp. Phase I/II prospective trial of autologous platelet tissue graft in gynecologic surgery. J. Minim. Invasive Gynecol. 2007; 14: 633–637.
15. Cook J.L., Purdam C.R. Is tendon pathology a continuum? A pathology model to explain the clinical presentation of load-induced tendinopathy. Br. J. Sports Med. 2009; 43: 409–416.
16. de Vos R.J., Weir A., van Schie H.T. i wsp. Platelet-rich plasma injection for chronic Achilles tendinopathy: a randomized controlled trial. JAMA 2010; 303: 144–149.
17. Peerbooms J.C., Sluimer J., Bruijn D.J., Gosens T. Positive effect of an autologous platelet concentrate in lateral epicondylitis in a double-blind randomized controlled trial: platelet-rich plasma versus corticosteroid injection with a 1-year follow-up. Am. J. Sports Med. 2010; 38: 255–262.
18. Krogh T.P., Fredberg U., Stengaard-Pedersen K. i wsp. Treatment of lateral epicondylitis with platelet-rich plasma, glucocorticoid, or saline: a randomized, double-blind, placebo-controlled trial. Am. J. Sports Med. 2013; 41: 625–635.
19. Kon E., Buda R., Filardo G. i wsp. Platelet-rich plasma: intra-articular k nee injections produced favorable results on degenerative cartilage lesions. Knee Surg. Sports Traumatol. Arthrosc. 2010; 18: 472–479.
20. Patel S., Dhillon M.S., Aggarwal S., Marwaha N., Jain A. Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. Am. J. Sports Med. 2013; 41: 356–364.

21. Nin J.R., Gasque G.M., Azcarate A.V., Beola J.D., Gonzalez M.H. Has platelet-rich plasma any role in anterior cruciate ligament allograft healing? Arthroscopy 2009; 25: 1206–1213.
22. Adamski Z., Kaszuba A., editors. Dermatologia dla kosmetologów. Wrocław, Elsevier Urban & Partner 2010.
23. Callan A., Zdrowa skóra. Kraków, Wydawnictwo Medycyna Praktyczna 1999.
25. Bielecki T , Gazdzik TS, Arendt J et al. Antbacterial effect of autologous platelet gel enrich with growth factors and other active substances. In vitro study. J Bo Surg Br 2007; 89 :417-420.
25. Kim J., Park C., Park H.: Curative effect of autologous platelet-rich plasma on a large cutaneous lesion in a dog. Vet. Dermatol. 2009, 2, 123-126.
26. Kostrzewski M., Aleksiewicz R., Kostrzewa D., Kostro K., Lutnicki K.: The use of hyaluronic acid and autologous platelet-rich plasma in canine degenerative knee joint disease and anterior cruciate ligment injury. Wet. Prakt. 2013, 4, 16-24
27. Pietramaggiori G., Schrerer S., Cervi D., Klement G., Orgill D.: Tumors stimulate platelet delivery of angiogenic factors in vivo. An unexpected benefi. Am. J. Pathol. 2008, 9, 1609-1616.
28. Gołas A., Treliński J., Kliniczne zastosowanie osocza bogatopłytkowego, Hematologia 2014; 5: 256.