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Correlation between the composition and effects of platelet rich plasma in tissue regeneration applications

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Abstract

Platelet rich plasma is a platelet concentrate derived from whole, autologous blood, which is rich in molecules known as growth factors. Since its discovery, platelet rich plasma has been proven to promote cellular proliferation, cell differentiation and, most importantly, wound healing. Its large range of application varies from skin rejuvenation to the treatment of cutaneous ulcers, deep wounds or diabetic foot lesions. In this review, we have summarized platelet rich plasma's characteristics and composition and synthesized relevant data on its effect in different diseases and disease-caused wounds.

Keywords: platelet rich plasma, growth factors, wound healing, cell proliferation.

1. Introduction

Platelet-rich plasma (PRP) is a whole-blood (WB) derived concentrate which contains mainly a fraction of platelets and little to no plasma (H.I. WANG & al. [1], J. CHAHLA & al. [2]). PRP is known to influence cellular proliferation, tissue regeneration and wound healing (MARX [3]). It is rich in growth factors, which are molecules that are released when the thrombocytes are activated (ANITUA & al. [4]).

Even though studies regarding PRP have been conducted since 1954 (KINGSLEY [5]), it is only as late as 1978 that studies on PRP's effect on wound healing started to develop (THORGEIRSSON & al. [6]). Even though the vast majority showed positive results for the use of PRP in clinical applications, there is still need to explore the mechanisms triggered by PRP and more animal and human clinical trials on this topic are required (YU & al. [7]; ALSOUSOU & al. [8]; AFRADI & al. [9]).

Even though the PRP is used mainly for medical purposes, it actually has a much wider sphere of applications, such as in dermatocosmetology – it can be used in skin rejuvenation, as it stimulates the synthesis of type I collagen (KIM & al. [10]; ABUAF & al. [11]), in the treatment of androgenic alopecia – as it stimulates hair growth and promotes the hair follicle regeneration (ALSOUSOU & al. [8]; ANITUA & al. [12]) or the treatment of diabetic foot ulcer (Ahmed & al. [13]). In addition to its beneficial effect on the biological processes mentioned above, PRP can also be used for its anti-inflammatory properties (WANG & al. [14]) and has the advantage of being inexpensive, autologous and readily available (WANG & al. [1]).

The aim of the present review was to emphasize the effects and influence of PRP on wound healing and tissue regeneration processes, considering the composition of PRP, the role of growth factors found in PRP, its effect on cellular proliferation and differentiation processes.

2. Composition and characteristics of PRP

The quantity of PRP obtained (and its final therapeutic effect, as well as the PRP composition) varies on a series of factors, such as the volume of blood collected and processed, the activation method, the platelet count and, of course, the individual variability of each patient.

There are various methods to obtain PRP –but there are no standardised procedures. The most common procedures of obtaining PRP are either using a special kit (KREUZ & al. [15]), or centrifuging the samples (FOSTER & al. [16]). The final product can vary in composition, and it can be pure PRP (P-PRP) or leucocyte-rich PRP (L-PRP) (DOHAN EHRENFEST & al. [17]; ARSHDEEP & al. [18]).

When working with whole-blood (WB), it is adequate to use an anticoagulant, in order to avoid coagulum formation, to inhibit the blood-coagulation cascade (FOSTER & al. [16]) and to be able to work with the blood samples, but also in order to avoid platelet activation before its use. Some methods require the blood to be collected in ethylenediaminotetraacetic acid (EDTA) coated tubes, other suggest the blood should be collected in sodium citrate (SC) tubes and that the resulting PRP fraction should be activated (Afradi & al. [9]).

In order to counterattack the effect of the anticoagulant, activators are used so as to force the platelets to release growth factors. The most popular activators are thrombin, calcium chloride, and type I collagen, but their concentration is vital and different concentrations can determine different results. It is known that type I collagen generates a poor growth factor release, while thrombin and calcium chloride (as well as calcium chloride mixed with thrombin) are more stable and provide an increased growth factor release (CAVALLO & al. [19]). In general, the saline solution of calcium chloride and thrombine is used in a 10% concentration (YU & al. [7]), while calcium chloride is commonly used in a 20 mM concentration (AFRADI & al. [9]). Even though there is an abundance of researchers that support the use of platelet activators, there are also multiple authors that authors do not activate the platelets before using them (DHURAT & al. [20]). For instance, a study that investigated the effect of PRP on the proliferation of adipose derived mesenchymal stem cells obtained positive results without using any type of platelet activator (ATASHI & al. [21]). A study on the effect of PRP on hair loss compared the effect of inactivated PRP and activated PRP, and the results showed that the patients that received inactivated PRP recorded a bigger increase in hair density compared to the activated PRP (GENTILE & al. [22]).

Even though, in general, PRP is used in liquid form, it can also be used in powder form, which has the advantage of having longer effect and being more consistent in growth factors (KIEB & al. [23]). Other researchers also reported the uses of PRP in gel form, which can be more effective than an antiseptic since it displays antibacterial properties (BIELECKI & al. [24], RODRIGUEZ & al. [25], AHMED & al. [13]). To apply an adequate and satisfactory quantity of growth factors and cytokines (KIEB & al. [23]) or tissue repair, it is crucial for physicians to find a method that allows the control and injection of an exact amount of PRP. Generally, it is recommended that each PRP application should be tailored for individual needs, instead of one standardized dose (WANG & al. [14]), independent on the envisaged regeneration application.

3. Molecules found in PRP with beneficial effects for tissue regeneration processes

It is known that the platelets have in their composition a number of different granules: α-granules, dense granules and lysosomes. The α-granules contain a series of molecules involved in wound healing and inflammation, such as the transforming growth factor β1 (TGF-β1), the fibroblastic growth factor (FGF), the epidermal growth factor (EGF), the vascular endothelial growth factor (VEGF), the platelet-derived growth factor (PDGF) and the

insulin-like growth factor (IGF), that need to be released so as to achieve their function (BLAIR & al. [26]; RUMBAUT & al. [27]). In vivo, when platelets with intact endothelium are circulating through the vessels, they are in an inactivated state; if a lesion appears and the endothelium breaks, the platelet encounter molecules that set off their activation (figure 1), such as collagen or thrombin, that are used in vitro as activators, and thus triggers the release of growth factors and other molecules contained by the granules (YUN & al. [28]).

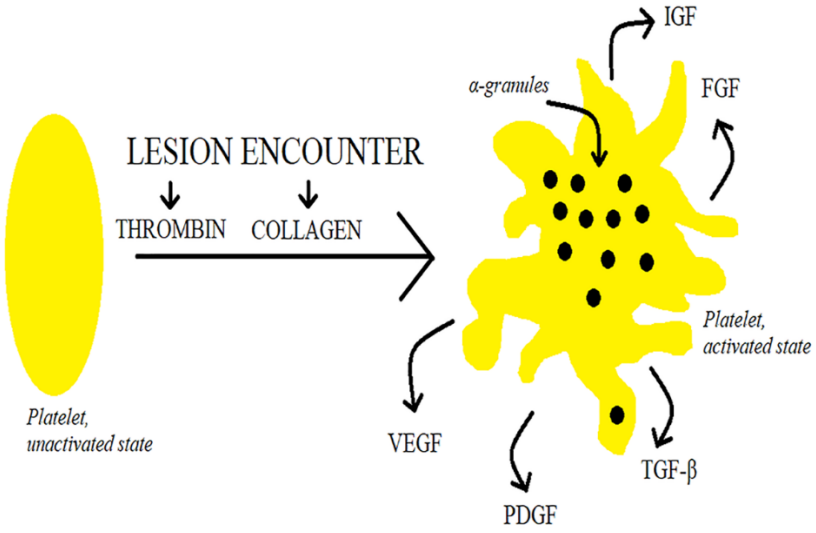

Fig. 1: The platelet activation mechanism; When the platelets are activated, they release growth factors and other molecules.

The growth factors found in PRP co-interact in complex networks, underlying main cellular processes such as proliferation, tissue regeneration and wound healing (HUANG & al. [29]; GEORGAKOPOULOS & al. [30]; LEE & al. [31]). The concentration of growth factors depends on the PRP obtaining method (MARX [3]) and on the type of application used (CASTILLO & al. [32]; KUSHIDA & al. [33]; KIEB & al. [23]). A diversity of studies analyses and compares growth factors concentration found in human blood and PRP (table 2).

Table 2. Comparison between the growth factors concentration from blood and PRP (according to EPPLEY & al. [34], ALSOUSOU & al. [8]).

Growth factor	EPPLEY & al. [34]		ALSOUSOU & al. [8]
	Blood (ng/mL)	PRP (ng/mL)	PRP (ng/mL)
TGF-β1	35±8	120±42	169.4±84.5
PDGF-AB	-	-	117.5±63.4
PDGF-BB	3.3±0.9	17±8	9.9±7.5
IGF	-	-	84.2±23.6
VEGF (pg/mL)	155±110	955±1030	-
EGF (pg/mL)	129±61	470±317	-

A study (WEIBRICH & al. [35]) conducted on 158 males and 55 females aged 17 to 62 concluded that the growth factors' concentration in PRP was not influenced by the donors' age or sex, except the IGF-1, where it was observed a slight decrease in concentration with age. As mentioned before, a key factor to the growth factors' concentration in PRP is the patients' biological condition, which is directly responsible for the platelet count, even if

some researchers allude that it is not yet fully characterized and does not influence the growth factors' concentration (WEIBRICH & al. [35]).

Being one of the first growth factors identified (CASATI & al. [36]; FERNANDES & al. [37]), PDGF has been discovered to have multiple isoforms, but their exact role has not been established yet (MARX [3]). PDGF is actively involved in angiogenesis (YU & al. [7]) and in stimulating the fibronectin, collagen and hyaluronic acid synthesis (SERVOLD [38]; FERNANDES & al. [37]), thus, it plays an important role in tissue regeneration and wound healing (CASATI & al. [36]; FERNANDES & al. [37]). Certain studies proved that the application of PDGF at the wound site decreases the wound's healing time (CANALIS & al. [39]; FERNANDES & al. [37]). It has been observed that PDGF can be found in 3 isoforms: AA (αα), BB (ββ), or AB (αβ) (MARX [3]).

The second most frequent growth factor found in PRP is TGF-β1 (WRANA [40]; FERNANDES & al. [37]) which stimulates angiogenesis, cell proliferation (stem cells and keratinocytes), extracellular matrix (along with collagen type I and type II) synthesis (DHURAT & al. [20]; FRAUTSCHI & al. [41]). Being a polypeptide and having multiple isoforms (ASSOIAN & al. [42]; YU & al. [7]), TGF-β1 and its receptors are found in almost all tissue types (WRANA [40]; KHALIL [43]). This specific isoform (TGF-β1) has a peak immediately after the wound is created, which suggests that the β1 isoform has a central role in the process of wound healing (ROBERTS [44]; FRANK & al. [45]). It is safe to assume that TGF-β1 plays a key role in the wound healing process since this growth factor influences the synthesis of type I and type III collagen in the extracellular matrix, promotes the replacing of type III collagen with type I collagen in the wound strengthening process and stimulates the fibroblasts differentiation to myofibroblasts during the wound healing process (PIERCE & al. [46]; HATA & al. [47]). A study conducted on 64 rats evaluated the effect of TGF-β on healing the tendon-to-bone insertion (KIM & al. [10]). At the end of the study, the group that received TGF-β injections at the repair site showed an increased type III collagen production, compared to the control group that received saline solution, suggesting that TGF-β plays an important role in tissue remodeling and wound healing.

One of the angiogenic factors, stimulating the blood vessel formation and angiogenesis, VEGF also plays an important role in cellular proliferation and endothelial cell migration (AHANI & al. [48]). The hypothesis that VEGF is able to stimulate the wound healing process is widely accepted by scientists for the reason that VEGF promotes re-epithelialization, microvessel formation and collagen deposition in the wound (LEE & al. [31]; YU & al. [7]).

An important part in growth regulation and differentiation processes in certain types of tissues is played by IGF, which can be found in several sources, such as stem cells, monocytes, capillaries, osteoblasts and skeletal muscles (MCCARTHY & al. [49]; YU & al. [7]; CLATICI & al. [50]; FERNANDES & al. [37]). If IGF and growth hormones are administrated combined, they have a positive effect on tissue regeneration, stimulating the wound healing process (UELAND [51]; FERNANDES & al. [37]).

Found in platelets, chondrocytes, mesenchymal cells, osteoblasts and macrophages (LEE & al. [31]), FGF is involved in the stimulation of embryonic development, tissue repair and wound healing (YU & al. [7]). It has been observed that the expression of FGF peaks after inducing an injury, and, in consequence, it can be clinically efficient in wound healing, particularly in cutaneous wounds, including chronic ulcers and diabetic wounds (TANG & al. [52]).

One of the growth factors that plays an important role in the stimulation of endothelial angiogenesis, EGF also plays a role in the regulation of collagen secretion, thus having an indirect impact on cellular proliferation and tissue regeneration (FABI & al. [53]; FRAUTSCHI & al. [41]).

Apart from growth factors, other molecules with important effect are found in PRP, such as interleukins (IL), such as IL1β, IL-6, IL-8, IL-10, monocyte chemotactic protein 1 (MNP-1), tumor necrosis factor α (TNF-α) (POCHINI & al. [54]), fibrin, fibronectin and vitronectin (MARX [3]). Along with the growth factors in PRP, there are anti-inflammatory cytokines, such as IL-1 receptor antagonist (RA), IL-5 and IL-10, that have a substantial effect on the wound healing process (AMABLE & al. [55]).

4. PRP influence on cellular proliferation and differentiation

Numerous studies show that PRP stimulates the proliferation of different kinds of cells, such as stem cells, dermal fibroblasts (KAKUDO & al. [56]), myofibroblasts (KUSHIDA & al. [33]), keratinocytes (STESSUK & al. [57]), retinal glial cells (CASTELNOVO & al. [58]), endothelial cells (BERTRAND-DUCHESNE & al. [59]). While it can be added to the culture medium to increase the cell proliferation rate (KAKUDO & al. [56]; LIAO & al. [60]), PRP can also be added into the culture medium replacing the fetal bovine serum, the results showing that this technique is biocompatible and stimulates the cell proliferation (ATASHI & al. [21]).

It has been observed that a concentration of 5% PRP added to the cells efficiently promoted proliferation (TAVASSOLI-HOJJATI & al. [61]), while high concentrations have the opposite effect on cellular proliferation (CHOI & al. [62]).

PRP treatment stimulates, in vitro, the proliferation and migration of retinal glia, which highlights the fact that PRP can be a very useful and effective tool in re-epithelialization and wound healing (CASTELNOVO & al. [58]).

In a study (KAKUDO & al. [56]) that evaluated the impact of PRP on cellular proliferation, adipose-derived stem cells (collected from human abdominal subcutaneous fat) and human dermal fibroblasts were harvested from the same patient, and the PRP was collected from 5 healthy donors. Cells were analyzed at 1, 4 or 7 days, and it was observed that the presence of PRP in the medium promoted cellular proliferation, which supports the idea that PRP application enhances the wound healing process.

The effect of conditioned medium from adipose-derived stem cells in combination with PRP on fibroblasts and keratinocytes was analyzed. It was concluded that low concentration of PRP stimulates cell proliferation and it has been suggested that the use of PRP has potential for re-epithelialization of lesions and wound healing (STESSUK & al. [57]).

It has been observed that, in vivo, PRP stimulates the cellular differentiation process, particularly osteogenesis and chondrogenesis. Bone-marrow stem cells interact well with different concentrations of PRP, which demonstrates that both of them can be engaged in regeneration of the bone. In this case, PRP leads to the proliferation of the cells and can increase the osteogenic differentiation in bone tissue, making it ideal for the early stages of wound healing (FERNANDES & al. [37]). Studies on the effect of PRP on muscle satellite cells were conducted on Sprague-Dawley rats in vitro as well as in vivo. In vitro, it has been observed that the cells treated with PRP presented a significantly enhanced cell proliferation, while in vivo it has been observed that the mice that received PRP treatment showed more osteogenic differentiation, more bone tissue with lamellar structure and fibrous tissue capsule. The study (HUANG & al. [29]) concluded that PRP was a very effective tool for bone tissue engineering, as it promoted muscle satellite cells proliferation and osteogenic differentiation.

5. The effect of PRP on tissue regeneration and wound healing process

As it is rich in growth factors that have been proved benefic in a large palette of applications, PRP is studied for its influence on tissue regeneration. One of the greatest advantages of using the PRP (compared to using alternative methods) is that the patients who

were administrated PRP presented no adverse effects, and the depth and length of the lesion showed a significant decrease (CROVETTI & al. [63]).

Wound healing is a process divided in four major stages (figure 2) that are partly overlapping, as follows: the first stage is hemostasis, followed by inflammation, cellular proliferation and finally, the fourth stage, tissue remodeling (TSANG & al [64]). This mechanism is coordinated by cellular interactions and diverse growth factors (HOVANET & al [65]; ZBUCHEA & al. [66]).

While in the first stage a blood clot is created by an aggregation of thrombocytes (which contain growth factors), the hemostasis stage partly overlaps with the inflammation stage, when the clot forms a barrier against microorganism invasion and will organizes the temporary matrix required for the next stage. In the first two phases, the growth factors that are responsible for promoting these processes are TGF-β1, FGF, VEGF and PDGF.

The proliferative stage begins within the first 48 hours after the lesion creation and can last for up to two weeks. In this stage, the angiogenesis occurs in the extracellular matrix and is crucial for the healing of the lesion, as this also includes re-epithelialization and cells' migration to the proximity of the wound.

The fourth stage starts 2-3 weeks after the onset of the wound and can last for up to one year. It depends on exogenous (such as smoking, different treatments) and endogenous (such as diabetes, venous stains) factors that can interfere with the healing process of the wound (GONZALEZ & al. [67]).

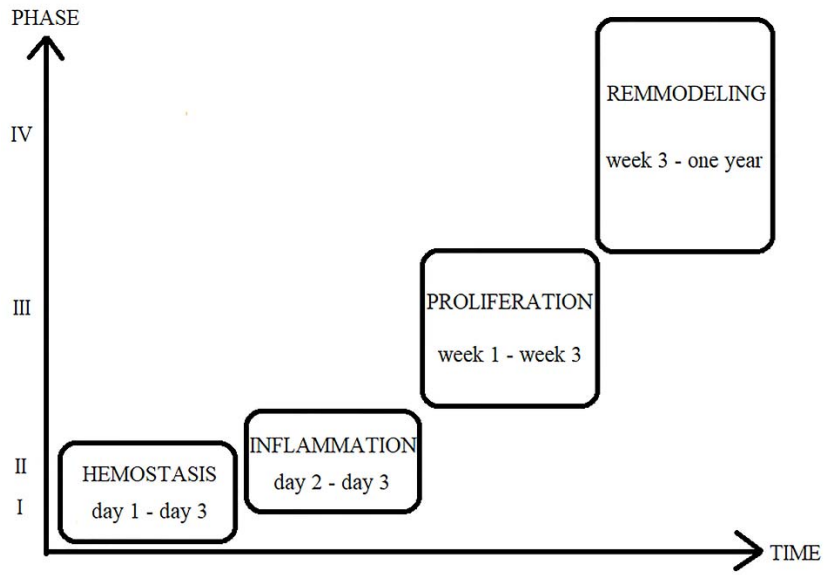

Fig. 2: **Wound healing approximate timeline**; It can be observed that the first two stages (hemostasis and the inflammatory phase) overlap, while the third and the fourth stage (proliferative phase, respectively tissue remodeling phase) are next to each other.

5.1. Effect on bone and connective tissue defects

PRP plays an important role in tendon and ligament regeneration due to the presence of PDGF, FGF and TGF-β1, that influence the cartilage oligomeric matrix protein and collagen synthesis (TAKAHASHI & al. [68]; LYRAS & al. [69]; SANCHEZ & al. [70]; ALSOUSOU & al. [8]).

A study (TAKAMURA & al. [71]) has been conducted on 50 rabbits with severed Achilles tendon. They were divided into 2 groups (one group received PRP treatment and one group received no treatment) in order to evaluate the effect of PRP on wound healing and its impact on wound healing stages. It has been observed that the PRP-treated group had a significant higher number of fibroblasts, their collagen fibers were denser, which all indicate tendon maturation. It has been highlighted that PRP had a positive effect on wound healing stages- it shortened the inflammatory phase and promoted tendon healing in the third, proliferative stage. Similarly, studies on New Zealand White rabbits showed that, after a severe injury on the Achilles tendon, the lesion healed faster if treated with PRP. The group that was treated with PRP displayed accelerated healing wounds and better histological quality of the scar tissue, compared to the control group (LYRAS & al. [72]).

Regarding PRP's effect on Greater Trochanteric Pain Syndrome, a clinical trial was conducted on 30 patients (24 females, 6 males) suffering from tendinosis, divided in 2 groups: 15 patients received PRP treatment, while the other 15 patients received percutaneous tendon fenestration. At the end of the study, even though there was no significant difference between the two groups regarding the healing process, the group treated with PRP claimed a lower, better pain score (JACOBSON & al. [73]).

Due to its wound healing properties, PRP is used in knee surgeries, ligament reconstruction, meniscal surgeries and chondral surgeries (SANCHEZ & al. [74]). Concerning knee-related surgeries, the scientific proposition is the use of intraarticular injections of PRP. For example, one treatment proposal suggests injecting PRP in small units of 5 mL (FILARDO & al. [75]), while others advise injecting approximately 2 mL of activated PRP (SANCHEZ & al. [76]). The case report is on a 12-year old athlete that was diagnosed with avulsion of knee articular cartilage and received an injection of 2 mL PRP; after the surgery, the patients' recovery was completed in 38 weeks, without recurrent symptoms (SANCHEZ & al. [76]).

Focusing on knee degenerative conditions, another 2-year study (FILARDO & al. [75]) on the effect of intra-articular PRP knee injection conducted on 90 patients suffering from chronic knee degenerative condition (some patients presented bilateral lesions) reached to the conclusion that, while further studies are needed, PRP is effective in reducing the pain, promoting the wound healing process and increasing the knee functionality.

Also, PRP helps relieving the pain of tibiofemoral cartilage degradation (HART & al. [77]), and it has been proved that the growth factors in PRP (especially TGF-β1) play an important role in fixing the lesions between the bone and the cartilage (KIM & al. [10]).

Fifty patients affected by chondromalatia received PRP treatment in the form of 9 injections over the course of a year and, at the end of the trial, they reported a significant improvement in pain reduction, even if the treatment did not influence the cartilage condition (HART & al. [77]).

Patients with dehiscent sternal wounds that were treated with PRP showed significant improvement by reducing the healing rate (3.5 weeks compared to 6 weeks), and also showed no noticeable side effects. The patients were chosen based on the fact that their wounds were difficult to heal and received a treatment with PRP in gel form (MAZZUCCO & al. [78]).

Another effect of PRP is that it aids regenerating the bone tissue (WEI & al. [79]), relieving the pain of patients suffering from osteoarthritis, improving the quality of their joints and helping them regain flexibility, thus proven to be more efficient compared to the hyaluronic acid that had been used before (RAEISSADAT & al. [80]; UPCHURCH & al. [81]; SATURVEITHAN & al. [82]). PRP is also very useful in the treatment of degenerative scoliosis, herniated disc and pseudoarthrosys, reducing the healing time needed after the repair surgery (HEE & al. [83]).

Furthermore, a clinical trial (GEORGAKOPOULOS & al. [30]) analyzed the effect of PRP in bone formation around loaded dental implants and evaluated 30 patients (aged 25 to 60), that were divided in 2 groups- 15 patients received PRP treatment around the new dental implants, while the other 15 patients did not receive any treatment. The study demonstrated that the PRP application enhanced bone regeneration dynamics and influenced positively bone formation.

5.2. Effect on cutaneous tissue wounds

The effect of PRP on wound healing has been intensely researched since 1990, when a platelet-derived wound healing formula was believed and proven to be efficient in promoting the repair of the lesion by stimulating the epithelialization of the wound (KNIGHTON & al. [84]). It has been observed that, if treated with PRP, the re-epithelialization process occurs during the wound healing at a much faster rate, compared to the wounds that did not receive PRP treatment (LAW & al. [85]).

There is a certain number of studies that show the effect of PRP on epidermal tissue wounds. A clinical trial (CROVETTI & al. [63]) on the effect of PRP in gel form on wound healing evaluated a total of 24 patients suffering from cutaneous ulcers with different ethiopathogenesis that received one application of PRP gel per week. At the end of the study it has been concluded that PRP promoted wound healing, as most of the patients presented re-epithelialization (some patients even achieved complete re-epithelialization) and that PRP also helped reducing the pain. A 3-year clinical trial (AFRADI & al. [9]) evaluated 100 patients (67 males and 33 females, median age of 27, respectively 33) suffering from thalassemia leg wounds that received treatment with 1 mL of autologous PRP-gel. The re-epithelialization of the wound took 4 weeks in average, while after 14 weeks the wound healed completely.

One of the first reports regarding the use of PRP with the purpose of treating non-healing skin ulcers had remarkable results, in some cases 100% healing rate being achieved. In this early study patients that had unhealed wounds for a large period of time (from 12 to 156 weeks) were evaluated, but after the PRP treatment the wounds healed quickly (3 to 19 weeks) and completely (ATRI & al. [86]). PRP treatment was found to be effective, quickening the healing process and also reducing the lesion's dimensions by approximately 70% (ANITUA & al. [87]).

It has been established that PRP is an effective, quick and safe tool in the treatment of diabetic foot ulcer, diminishing even the non-healing wounds, and having no side effects. This study evaluated 129 patients suffering from type I or type II diabetes and they were subjected to a 7-day screening period; the patients were divided in two groups- one group that received PRP treatment, and one group that received a saline gel dressing, named the control group. The group that received PRP treatment had smaller and thinner wounds that healed faster and did not present any adverse effect that was treatment-related, compared to the control group (DRIVER & al. [88]), thus proving that PRP treatment is very powerful in the management of wound healing.

It has been discovered that PRP is very effective in the treating of ulcers caused by leprosy- the treatment with PRP leads to quick wound healing, thus reducing the treatment's duration, while the healing process has no correlations with the size or the leprosy spectrum of the ulcer (ANANDAN & al. [89]). The study evaluated 50 patients suffering from grade II of Wagner's ulcer classification, from whom, after the PRP treatment, 46 patients presented complete wound healing and the remaining 4 patients showed only partial re-epithelization, as their wounds reduced in size, proving once again that PRP treatment is extremely effective if used for wound healing.

Due to its antibacterial properties, PRP is able to clean the wound of microorganisms and to simultaneously heal it (WANG & al. [90]). A study (CIESLIK-BIELECKA & al. [91]) on patients suffering from acquired immune deficiency syndrome discovered that PRP has a positive effect on crural chronic ulcers, while it also brought complete wound closure and cleaned the wounds of microorganisms like *Staphylococcus aureus* and *Pseudomonas aeruginosa.*

5.3. Effect on other tissues defects

A study (MOGHADAM & al. [92]) was performed to evaluate the effect of PRP on kidney regeneration in case of nephrotoxicity. The animals received for 8 days 80mg/kg of gentamicin with the purpose of inducing nephrotoxicity, and were treated with one dose of 100μL injected PRP. At the end of the study, one kidney in each rat was sectioned and it has been observed that PRP positively influenced the proliferation of epithelial cells in convoluted tubules and improved the gentamicine-induced fibrosis.

Animal studies showed that PRP has a benefic effect on peripheral nerve regeneration after nerve injury; the studies concluded that PRP has an immense potential for nerve regeneration, but more clinical trials are needed (YU & al. [7]).

Eye-drops that contain PRP were found to be effective in ophthalmology related wound healing, due to the growth factors found in PRP- the growth factors cocktail stimulates corneal epithelial migration and proliferation, corneal wound healing, retina repair (ANITUA & al. [93]) and promotes stromal repair process, thus being successfully used in the treatment of ocular surface syndrome and restoring the lacrimal function of the lacrimal gland (ALIO & al. [94]; AVILA [95]; ANITUA & al. [96]). In addition, PRP stimulates the wound healing of epithelial corneal cells, promotes the wound healing after photo ablation surgery and reduces the haze formation (ANITUA & al. [97]), while it also diminishes scar formation on the ocular surface (ANITUA & al. [98]) and is effective in the treatment of ocular chemical burns (SHARMA & al. [99]).

The impact of PRP treatment on ocular surface syndrome (after laser eye surgery) was evaluated through a clinical trial conducted on 13 patients (26 eyes; 9 females and 4 males). The patients received a treatment that consisted in autologous PRP eye-drops and one patient developed intolerance to PRP after 4 weeks. After the study, it was reported that PRP eye-drops had a positive effect on punctate keratitis and the patients claimed that their symptoms were generally relieved (ALIO & al. [94]).

6. Conclusions

Due to its content in growth factors and anti-inflammatory molecules, PRP is able to stimulate the cellular proliferation and migration process, to promote the tissue regeneration, to enhance the wound healing, to quicken the healing process and reduce scar formation. Further clinical trials are necessary in order to establish PRP's mechanism of action and role in essential cellular processes.

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