Exokine and the Youth-Boosting Treatment Based on One's Own Serum: Wheat and Chaff

Philippe Magistretti, MD[1] Dario Bertossi, MD, PhD[2] Ali Pirayesh, MD[3] Alessandra Magistretti, MS[4] Salvatore Chirumbolo, PhD[5]

[1] Summit Clinic Crans Montana, Switzerland
[2] Department of Surgery, Dentistry, Paediatrics and Gynaecology and Head of Maxillofacial Plastic Surgery Unit, University of Verona, Italy
[3] Amsterdam Plastic Surgery, Amsterdam, The Netherlands
[4] School of Medicine, University of Verona, Italy
[5] Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Italy

Address for correspondence Salvatore Chirumbolo, PhD, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Strada Le Grazie 9 37134 Verona, Italy (e-mail: salvatore.chirumbolo@univr.it).

Facial Plast Surg 2022;38:177–181.

Abstract

Within the field of skin rejuvenation, clinicians have broadened the application of proven therapies toward antiaging medicine. Specifically, both platelet-rich plasma (PRP) and autologous-conditioned serum (ACS) have received great consideration among experts for novel indications. While the medical research focused on ACS is strengthened in their evidence and supported by promising outcomes, much more debates exist regarding the efficacy of PRP. Despite limited supporting literature to date, physicians and surgeons should be encouraged to explore the use of these approaches and in shedding further light on their potential benefits by contributing new evidence from basic and clinical scientific investigation.

Keywords
- platelet-rich plasma
- autologous serum
- rejuvenation
- PRP
- aesthetic medicine

Within the field of skin rejuvenation, current strategies have endowed clinicians with novel opportunities of application for these proven tools. Specifically, both platelet-rich plasma (PRP) and autologous-conditioned serum (ACS) have received great consideration among experts for the use in antiaging regimens. So far, worldwide information about aesthetics is claiming the existence of a new promising way to reverse the aging process on skin through focused therapy directed at and the effects of thinning Specifically, the simple use of one's own incubated serum or PRP is a proposed method for achieving antiaging benefits. This attempt might simply be described, therefore, as the use of an autologous blood extract, for example, PRP or ACS, which are both particularly enriched in biomolecules and growth factors and adapted for skin rejuvenation and musculoskeletal disorders.[1] Briefly speaking, the idea is particularly encouraging and appealing; however, given the limited supporting literature, it must be determined if we are dealing with a myth or a real opportunity.[1]

Actually, skin rejuvenation by using PRP is highly controversial, as it seems that the majority of clinical case studies are scientifically inconsistent and unreliable, with respect to the more rigorous open randomized clinical trials.[1] A possible reason is the puzzling complexity of actions associated with autologous PRP, which renders any good experimental and scientific attempt an empirical approach.[2,3] Yet, Lei et al, in a systematic review on a total of 108 articles, reported that PRP should play a major role in tissue rejuvenation.[4] Despite some encouraging evidence, further research is needed, however, as contradictory evidence was also reported.[5–7] As a matter of fact, the term Exokine (or Exokine-Serum) is a commercial translation of autologous transfer of plasma or serum, which is used in numerous healthcare structures, held for aesthetics purposes to get skin rejuvenation. Examples of Exokine application are shown in ►**Figs. 1** to **3** in this article.

To explain the biological role of PRP in tissue rejuvenation, plasma or serum should be finely characterized in their

published online
April 22, 2022

Issue Theme Nonsurgical Facial Treatments; Guest Editor: Dario Bertossi, MD, PhD

Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA

DOI https://doi.org/10.1055/s-0042-1747970.
ISSN 0736-6825.

Fig. 1 Case 1: Treatment of the tear trough and of the nasolabial groove with filling effect. We injected 2 mL of Exokine with a 1 mL luer lock syringe and a 38 mm 25G cannula in both sides. Results at 3 weeks show lasting volumization and improved skin texture. Avant = before the treatment; Aprés = after the treatment.

biomolecular composition. In this sense, plasma and serum metabolomes were recently reported and obviously they depend on an individual's and populations' genetics.[8–10] Furthermore, the process of aging dramatically changes the presence of at least 100 different major metabolites over 300 unique substances recently reported in plasma metabolomics.[9] This evidence compels experts in the field to standardize PRP on the basis of its outcome on patients, not of its biological nature, an issue that leaves to PRP a certain degree of empiricism. Despite this, Banihashemi et al reported a mild-to-excellent amelioration in nasolabial fold, periorbital dark circles, skin rigidity, and periorbital wrinkles by using pure PRP facial injection in 30 female subjects.[11] Positive outcomes in periorbital dark circles by using PRP were reported also by other authors, who described the achievement of an increasing satisfaction score in treated patients.[12] Actually, current literature seems to support the use of PRP in the periorbital region, including crow's feet wrinkles.[13] Notwithstanding, the majority of PRP applications, as a

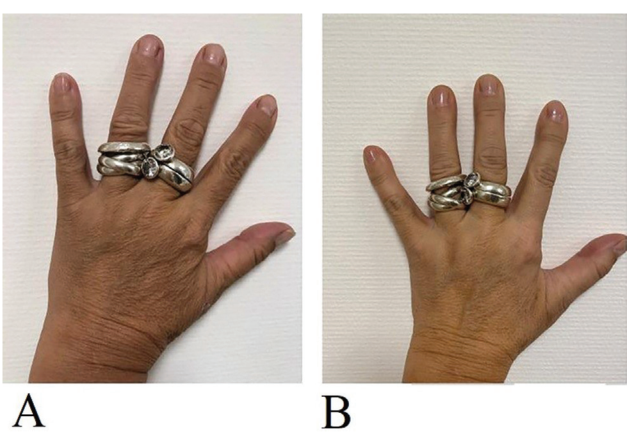

Fig. 2 Case 2: Treatment of the tear trough with filling effect. We injected 2 mL of Exokine with a 1 mL luer lock syringe and a 38 mm 25G cannula in both sides. Results at 3 weeks that show volumization of the area and most important, loss of pigmentation. Avant = before the treatment; Aprés = after the treatment.

Fig. 3 Case 3: Treatment of the back of the hands. We injected 4 mL of Exokine per side with a 1 mL luer lock syringe and a 38 mm 25G cannula. Results at 3 weeks show improved skin texture and elasticity. Avant = before the treatment; Aprés = after the treatment.

therapeutic approach, can be retrieved on musculoskeletal disorders.[14] The application of the Exokine Serum methodology includes therefore a wide umbrella of autologous transfer of blood derived products to ameliorate a plethora of illnesses or discomforts regarding skin, bone, or connective tissues.

Before expanding this issue further on, it is of the utmost importance to review and detail the biological nature and composition of PRP and ACS.

PRP Composition and Its Impact in Rejuvenation Medicine

A great deal of research has gone into the characterization of components present in PRP and ACS. So far, the spotlight was principally pointed onto the numerous growth factors present in PRP, such as epidermal growth factor (EGF), insulin-like growth factor 1 (IGF-1), hepatocyte growth factor (HGF), transforming growth factor β (TGF-β) vascular endothelium growth factor (VEGF), platelet-derived growth factor (PDGF), and fibroblast growth factor (FGF), most of which are indeed complex families of growth factors, more than single components.[15–18] A more recent renewed interest was yet devoted to exosomes present in PRP.[19] PRP exosomes (PRP-exos) are nanovesicles carrying a great deal of molecular factors, including biomolecules, microRNAs, transcripts, and proteins, and in this sense they play a major role in modulating plastic rejuvenation and tissue turnover.[19] This evidence suggests that the bioactivity of PRP is particularly complicated by the existence of a plethora of factors, each with complex interactions and functions. For example, FGFs, which have a major role in tissue rejuvenation, are represented by a complex family of growth factors, usually known as heparin-binding growth factors, because linking heparin,[20] which include acidic FGF (FGF-1), basic FGF (FGF-2), int-2 (FGF-3), hst/KS3 (FGF-4), FGF-5, FGF-6, keratinocyte growth factor (FGF-7), androgen induced growth factor (FGF-8), glia activating factor (FGF-9), and at least 23 different members of FGFs.[21–24] Discriminating the single activity of each FGF component in such complex milieu to follow the subsequent biomolecular and cellular events leading to skin rejuvenation is particularly burdensome, for obvious practical reasons.

However, the presence of skin microenvironments, epidermal, dermal, subdermal, or musculoskeletal, may differentiate actions depending on the depth of delivery of the active principles.[25] This practically prompts up possible strategies as different procedures and devices, activating skin rejuvenation at different depths. Usually, the quality of a PRP is evaluated via its total platelet amount (at least 4 times higher respect to the physiological content in whole blood) and platelet viability and functionality, measured by analyzing platelet aggregometry, thromboelastography, and flow cytometry.[26] Platelet α-granules produce fundamental growth factors such as PDGF, VEGF, TGF-β, and EGF. The amount and composition in growth factors of a PRP have been recently reported and may account on simple enzyme-linked immunosorbent assay test.[27] The role of these growth factors for tissue rejuvenation is of major importance. The regenerative effect of PDGF-BB has been reported on the dentin–pulp complex,[28] bone regeneration,[29] skin rejuvenation, and wound healing,[30] and even as a topical direct treatment.[31] The widespread idea about PRP quality is that its potential depends on the "proper" cocktail of growth factors components, most of which produced by platelets themselves.[15] What we would like to assess is that the use of PRP is an example of "autologous orthobiologics," a biological way used in medicine and surgery to renew and recover damaged or functionally impaired tissues accounting on the regenerative potential of autologous tissue transfer, such as haemoderivatives.[32] Hemoderivatives, for example, PRP, are functionally promising agents also in musculoskeletal disorders such as tenditopathies,[33,34] involving an anatomical district where is particularly effective also ACS.

PRP is enriched with growth factors by using a cavitation process (via sonication or ultrasonication) able to allow the release from platelets of the major growth factors with rejuvenation properties (►**Fig. 4**).[35] In this context, a wide plethora of different technological approaches can be retrieved from literature, which are able to produce PRP with commercial purposes.[36] The concentration of the different GF is lower in PRP samples compared with ACS. This is likely due to the fact that platelets in the former sample have not had the time to produce them. This circumstance represents the major shortcoming of PRP versus ACS as the uncertainty to the destiny of the platelets after the injection cannot be verified.

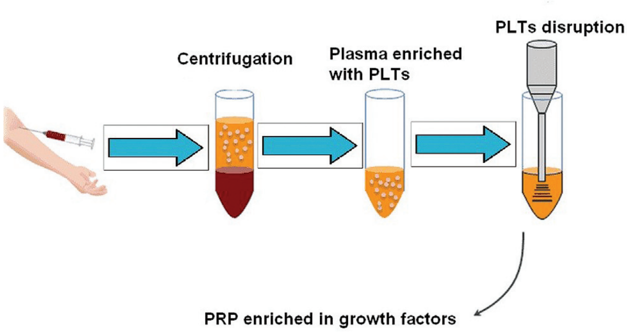

Fig. 4 A rapid summary on the basic mechanisms by which platelet-rich plasma (PRP) is prepared. PLTs, platelets.

Autologous-Conditioned Serum: Wheat and Chaff

ACS is a type of autologous serum enriched with IL-1-ra (interleukin 1-receptor antagonist) and is particularly used in rheumatic, osteoarthritic, and musculoskeletal disorders.[37] The usual content of ACS is its enrichment in IL-1ra, IL-10, TGF-β, associated with the presence of IL-6, tumor necrosis factor-α, oncostatin M, and IL-1β.[37] von Wehren et al successfully treated chronic Achilles tendinopathy with ACS.[38] These authors conducted a retrospective study with 50 patients undergoing only eccentric training who exhibited better VISA-A-G (Victorian Institute of Sport Assessment-Achilles questionnaire—German) following treatment with ACS, an indication of an improvement in their tendon functionality.[38] ACS therapy for tendinopathy works also in farm animals.[39] The biological activity of ACS, in that ACS is able to modulate the stem cell property of mesenchymal progenitors in the tissue, is of the utmost importance for the use of ACS in rejuvenation biomedicine.[40] Wehling et al who were the first to explore and use a pioneering form of ACS, named its use as "orthokine therapy"[41] and conceived a kind of autologous serum deprived of cells (cell-free) and treated on glass spheres.[41] Therefore, both Exokine and Orthokine are patented formulas, usually identifying a PRP or an ACS, used often for tissue regeneration (skin) the former and musculoskeletal disorders the latter. Actually, the use of ACS in veterinary science can account also on different technologies to produce them.[42,43] Typically, any rupture of the Achilles tendon can lead to slow rescue its full functionality and often incompletely recovery. Heisterbach et al, in Sprague-Dawley rat models, assessed that tendon healing was fundamentally exerted by BMP-12 and TGF-β1, besides ACS,[44] an experience of tendon healing reported also by others.[45]

At least in chronic knee osteoarthritis, ACS reported promising outcomes with respect to PRP.[46] Shirokova et al treated 123 patients suffering from osteoarthritis (Kellgren and Lawrence grade I to II) with PRP and ACS, reporting that at the 3-month follow-up ACS showed higher efficacy than PRP.[46] Wright-Carpenter et al used ACS in sport athletes with muscle strain and reported a shorter recovery time in comparison to the control group by approximately 6 months.[47]

The evaluation of ACS in skin rejuvenation was recently considered.[48] These authors wondered if a novel developed antiaging ACS, produced by using a particular syringe-like device which is able to expose autologous blood to medical-grade glass spheres, arranged in a closed system, was effective for skin rejuvenation.[48] Actually, the use of topical injected ACS gradually replaced also further approaches, such as directly topical application of growth factors.[49–51]

The role of ACS in tissue rejuvenation and wound healing appears undisputable, yet, are there concerns about the use of ACS in dermatology and skin rejuvenation?

The Orthoskin trial recently assessed that cell-free conditioned autologous serum in knee osteoarthritis and lumbar radiculitis on 21 female subjects ensured a significant improvement in cutaneous elasticity and skin firmness, reporting therefore an outcome in skin rejuvenation.[52] The effect of ACS, likewise PRP, depends on the way by which ACS is produced.[53] For example, efficiency in producing high-quality ACS depends on glass spheres or beads diameters (usually used altogether 2.0, 2.5, 3.5, and 4.0 mm diameters) and/or polished or coated with chromium sulfate, a way that allows blood-derived ACS to be enriched in IL-1-ra following 24 hours incubation with glass beads.[53] The commercial way with Exokine-Serum and Orthokine-Serum may provide the simplest solution to offering autologous hemoderivatives for tissue rejuvenation, and ultimately endowing surgeons with the proper technology.

Conclusions

What kind of message can we retrieve from this very short tale about PRP and ACS? The continuous development of new approaches to improve skin health, reduced aging-associated discomforts and damages, ensuring skin rejuvenation and tissue remodeling nowadays is referring to novel practices using autologous blood-derived products. Repair and rescue your health from yourself; this seems a very attracting message. While for ACS medical research seems much more strengthened in their evidence, supported by promising outcomes, much more debates are being arranged about the usefulness of PRP. Despite the possible criticisms raised around these products, physicians and surgeons should take advantage in their jobs by the use of these approaches and therefore they would be particularly encouraged in shedding further light on their use and development by adding new evidence from basic and clinical scientific investigation.

Authors' Contributions

D.B. and P.M. were involved in substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work. S.C. and D.B. were involved in drafting the work or revising it critically for important intellectual content. P.M., D.B., A.M., A.P., and S.C. gave final approval of the version to be published. P.M., D.B., A.M., A.P., and S. C. agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding

None.

Conflict of Interest

None declared.

References

1 Atiyeh B, Oneisi A, Ghieh F. Platelet-rich plasma facial rejuvenation: myth or reality? Aesthetic Plast Surg 2021;45(06):2928–2938
2 Creaney L. Platelet-rich plasma and the biological complexity of tissue regeneration. Br J Sports Med 2011;45(08):611
3 Mei-Dan O, Mann G, Maffulli N. Platelet-rich plasma: any substance into it? Br J Sports Med 2010;44(09):618–619
4 Lei X, Xu P, Cheng B. Problems and solutions for platelet-rich plasma in facial rejuvenation: a systematic review. Aesthetic Plast Surg 2019;43(02):457–469
5 Samadi P, Sheykhhasan M, Khoshinani HM. The use of platelet-rich plasma in aesthetic and regenerative medicine: a comprehensive review. Aesthetic Plast Surg 2019;43(03):803–814
6 Willemsen JC, van der Lei B, Vermeulen KM, Stevens HP. The effects of platelet-rich plasma on recovery time and aesthetic outcome in facial rejuvenation: preliminary retrospective observations. Aesthetic Plast Surg 2014;38(05):1057–1063
7 Kenworthy W, Langridge B, Patel N, Waterhouse N. Use of platelet preparations in facial rejuvenation and wound healing remains unproven. Aesthetic Plast Surg 2016;40(02):329–330
8 Psychogios N, Hau DD, Peng J, et al. The human serum metabolome. PLoS One 2011;6(02):e16957
9 Lawton KA, Berger A, Mitchell M, et al. Analysis of the adult human plasma metabolome. Pharmacogenomics 2008;9(04):383–397
10 Rhee EP, Yang Q, Yu B, et al. An exome array study of the plasma metabolome. Nat Commun 2016;7:12360
11 Banihashemi M, Zabolinejad N, Salehi M, Hamidi Alamdari D, Nakhaizadeh S. Platelet-rich plasma use for facial rejuvenation: a clinical trial and review of current literature. Acta Biomed 2021;92(02):e2021187
12 Mehryan P, Zartab H, Rajabi A, Pazhoohi N, Firooz A. Assessment of efficacy of platelet-rich plasma (PRP) on infraorbital dark circles and crow's feet wrinkles. J Cosmet Dermatol 2014;13(01):72–78
13 Kassir M, Kroumpouzos G, Puja P, et al. Update in minimally invasive periorbital rejuvenation with a focus on platelet-rich plasma: a narrative review. J Cosmet Dermatol 2020;19(05):1057–1062
14 Nazaroff J, Oyadomari S, Brown N, Wang D. Reporting in clinical studies on platelet-rich plasma therapy among all medical specialties: a systematic review of Level I and II studies. PLoS One 2021;16(04):e0250007
15 Pavlovic V, Ciric M, Jovanovic V, Stojanovic P. Platelet rich plasma: a short overview of certain bioactive components. Open Med (Wars) 2016;11(01):242–247
16 Boswell SG, Cole BJ, Sundman EA, Karas V, Fortier LA. Platelet-rich plasma: a milieu of bioactive factors. Arthroscopy 2012;28(03):429–439
17 Lubkowska A, Dolegowska B, Banfi G. Growth factor content in PRP and their applicability in medicine. J Biol Regul Homeost Agents 2012;26(2, Suppl 1):3S–22S
18 Kobayashi E, Flückiger L, Fujioka-Kobayashi M, et al. Comparative release of growth factors from PRP, PRF, and advanced-PRF. Clin Oral Investig 2016;20(09):2353–2360
19 Rui S, Yuan Y, Du C, et al. Comparison and investigation of exosomes derived from platelet-rich plasma activated by different agonists. Cell Transplant 2021;30:9636897211017833
20 Burgess WH, Maciag T. The heparin-binding (fibroblast) growth factor family of proteins. Annu Rev Biochem 1989;58:575–606
21 Wilkie AO, Patey SJ, Kan SH, van den Ouweland AM, Hamel BC. FGFs, their receptors, and human limb malformations: clinical and molecular correlations. Am J Med Genet 2002;112(03):266–278
22 Basilico C, Moscatelli D. The FGF family of growth factors and oncogenes. Adv Cancer Res 1992;59:115–165

23 Mossahebi-Mohammadi M, Quan M, Zhang JS, Li X. FGF signaling pathway: a key regulator of stem cell pluripotency. Front Cell Dev Biol 2020;8:79
24 Nunes QM, Li Y, Sun C, Kinnunen TK, Fernig DG. Fibroblast growth factors as tissue repair and regeneration therapeutics. PeerJ 2016; 4:e1535
25 Anitua E, Muruzabal F, Tayebba A, et al. Autologous serum and plasma rich in growth factors in ophthalmology: preclinical and clinical studies. Acta Ophthalmol 2015;93(08):e605–e614
26 Bausset O, Giraudo L, Veran J, et al. Formulation and storage of platelet-rich plasma homemade product. Biores Open Access 2012;1(03):115–123
27 Lee JW, Kwon OH, Kim TK, et al. Platelet-rich plasma: quantitative assessment of growth factor levels and comparative analysis of activated and inactivated groups. Arch Plast Surg 2013;40(05): 530–535
28 Zhang M, Jiang F, Zhang X, et al. The effects of platelet-derived growth factor-BB on human dental pulp stem cells mediated dentin-pulp complex regeneration. Stem Cells Transl Med 2017;6(12):2126–2134
29 Zhang M, Yu W, Niibe K, et al. The effects of platelet-derived growth factor-bb on bone marrow stromal cell-mediated vascularized bone regeneration. Stem Cells Int 2018;2018:3272098
30 Rajkumar VS, Shiwen X, Bostrom M, et al. Platelet-derived growth factor-beta receptor activation is essential for fibroblast and pericyte recruitment during cutaneous wound healing. Am J Pathol 2006;169(06):2254–2265
31 Rangarajan V, Dreher F. Topical growth factors for skin rejuvenation. In: Farage MA, Miller KW, Maibach HI, eds. Textbook of Aging Skin. Berlin, Heidelberg: Springer. Doi: 10.1007/978-3-540-89656-2_100
32 Dos Santos RG, Santos GS, Alkass N, et al. The regenerative mechanisms of platelet-rich plasma: a review. Cytokine 2021; 144:155560
33 Wagner RJ, Zach KN. Platelet-rich plasma injection for quadriceps tendinopathy: a case report. WMJ 2021;120(01):78–81
34 Liu X, Zhang R, Zhu B, et al. Effects of leukocyte- and platelet-rich plasma on tendon disorders based on *in vitro* and *in vivo* studies (Review). Exp Ther Med 2021;21(06):639
35 Wu Y, Kanna MS, Liu C, Zhou Y, Chan CK. Generation of autologous platelet-rich plasma by the ultrasonic standing waves. IEEE Trans Biomed Eng 2016;63(08):1642–1652
36 Kushida S, Kakudo N, Morimoto N, et al. Platelet and growth factor concentrations in activated platelet-rich plasma: a comparison of seven commercial separation systems. J Artif Organs 2014;17 (02):186–192
37 Rutgers M, Saris DB, Dhert WJ, Creemers LB. Cytokine profile of autologous conditioned serum for treatment of osteoarthritis, in vitro effects on cartilage metabolism and intra-articular levels after injection. Arthritis Res Ther 2010;12(03):R114
38 von Wehren L, Pokorny K, Blanke F, Sailer J, Majewski M. Injection with autologous conditioned serum has better clinical results than eccentric training for chronic Achilles tendinopathy. Knee Surg Sports Traumatol Arthrosc 2019;27(09):2744–2753
39 Geburek F, Lietzau M, Beineke A, Rohn K, Stadler PM. Effect of a single injection of autologous conditioned serum (ACS) on tendon healing in equine naturally occurring tendinopathies. Stem Cell Res Ther 2015;6(01):126
40 Blázquez R, Sánchez-Margallo FM, Reinecke J, et al. Conditioned serum enhances the chondrogenic and immunomodulatory behavior of mesenchymal stem cells. Front Pharmacol 2019;10:699
41 Wehling P, Moser C, Frisbie D, et al. Autologous conditioned serum in the treatment of orthopedic diseases: the orthokine therapy. BioDrugs 2007;21(05):323–332
42 Hraha TH, Doremus KM, McIlwraith CW, Frisbie DD. Autologous conditioned serum: the comparative cytokine profiles of two commercial methods (IRAP and IRAP II) using equine blood. Equine Vet J 2011;43(05):516–521
43 Sawyere DM, Lanz OI, Dahlgren LA, Barry SL, Nichols AC, Werre SR. Cytokine and growth factor concentrations in canine autologous conditioned serum. Vet Surg 2016;45(05):582–586
44 Heisterbach PE, Todorov A, Flückiger R, Evans CH, Majewski M. Effect of BMP-12, TGF-β1 and autologous conditioned serum on growth factor expression in Achilles tendon healing. Knee Surg Sports Traumatol Arthrosc 2012;20(10):1907–1914
45 Majewski M, Ochsner PE, Liu F, Flückiger R, Evans CH. Accelerated healing of the rat Achilles tendon in response to autologous conditioned serum. Am J Sports Med 2009;37(11):2117–2125
46 Shirokova L, Noskov S, Gorokhova V, Reinecke J, Shirokova K. Intra-articular injections of a whole blood clot secretome, autologous conditioned serum, have superior clinical and biochemical efficacy over platelet-rich plasma and induce rejuvenation-associated changes of joint metabolism: a prospective, controlled open-label clinical study in chronic knee osteoarthritis. Rejuvenation Res 2020;23(05):401–410
47 Wright-Carpenter T, Klein P, Schäferhoff P, Appell HJ, Mir LM, Wehling P. Treatment of muscle injuries by local administration of autologous conditioned serum: a pilot study on sportsmen with muscle strains. Int J Sports Med 2004;25(08):588–593
48 Pinto H, Garrido LG. Study to evaluate the aesthetic clinical impact of an autologous antiaging serum. J Drugs Dermatol 2013;12(03): 322–326
49 Gold MH, Goldman MP, Biron J. Human growth factor and cytokine skin cream for facial skin rejuvenation as assessed by 3D in vivo optical skin imaging. J Drugs Dermatol 2007;6(10): 1018–1023
50 Gold MH, Goldman MP, Biron J. Efficacy of novel skin cream containing mixture of human growth factors and cytokines for skin rejuvenation. J Drugs Dermatol 2007;6(02):197–201
51 Malerich S, Berson D. Next generation cosmeceuticals: the latest in peptides, growth factors, cytokines, and stem cells. Dermatol Clin 2014;32(01):13–21
52 Kerscher M. Cell-free autologous conditioned serum (ACS) improved skin elasticity: results of an investigator initiated clinical trial. Orthoskin I JADD 2017;76(06) Suppl 1:AB63
53 Magalon J, Bausset O, Veran J, et al. Physico-chemical factors influencing autologous conditioned serum purification. Biores Open Access 2014;3(01):35–38

