

Use of Platelet Rich Plasma in Otolaryngology-Review Article

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Abstract

The process of replacing or regenerating human cells, tissues, or organs to restore or establish normal function is known as REGENERATIVE MEDICINE. It is a brand new, developing field of medicine that deals with the functional repair of tissues or organs damaged by severe trauma or degenerative conditions. Currently, platelet-rich plasma (PRP) and stem cell-based treatments are the two competing technologies that can heal and restore the injured tissues. Platelet-rich plasma (PRP) applications used in new autologous cellular therapeutics have the potential to supplement a range of regenerative medicine therapy regimens [1]. An emerging and effective treatment alternative in musculoskeletal therapy is platelet-rich plasma (PRP). PRP is an autologous plasma preparation that has been enhanced with platelet concentrations above those seen in whole blood ordinarily. High platelet concentration has therapeutic promise because of their ability to give supraphysiologic levels of vital growth factors, which operate as a regenerative stimulus to encourage repair in tissues with poor healing capabilities [2]. A concentration of platelet-rich protein generated from blood that has been spun to remove the red blood cells is known as platelet-rich plasma (PRP), or more accurately autologous conditioned plasma. Despite being advertised to cure a variety of medical ailments, there is conflicting evidence for profit as of 2020, with some evidence supporting usage in some circumstances and opposing use in other. A unique substance that is being employed in several surgical specialties is platelet-rich plasma. The aim of the article is to review the ongoing and prospective utilization of platelet-rich plasma in the field of Otolaryngology [3].

Keywords: regenerative medicine; platelet rich plasma; stem cell therapy; therapeutic potential; healing, growth factors

Introduction

Platelet Rich Plasma

Platelet-rich growth factor (GF)/ Platelet-rich fibrin matrix (PRF)/ Platelet concentrate are the other names of Platelet rich plasma. Haematology started with the concept and description of PRP [4]. In 1970, haematologists created the term platelet-rich plasma so as to describe the plasma with platelet count above the peripheral blood used as a transfusion product for the treatment of thrombocytopenia [5]. PRP was first used in 1987 in an open-heart surgery ten years later, it started to be used in maxillofacial surgery as PRF. The haemostatic properties and ability of adherence was due to Fibrin. The cell proliferation was stimulated by the anti-inflammatory action of PRP [6]. With advancement, PRP was started to be used in the field of musculoskeletal system in sports injuries. The professional sportspersons experienced their early recovery hence PRP was attracted and widespread in the media and its uses grow exponentially. The other medical fields, namely Cardiology, Paediatric surgery, Gynaecology, Urology, Plastic surgery and

Ophthalmology [7]. The recent interest of PRP is its application in dermatology, right from alopecia to skin rejuvenation, it has shown tremendous results due to its property of wound healing which revisions the scar and tissue regeneration [8]. PRP is nothing but a biological product having a fraction of plasma of autologous blood with a concentration of platelet above the baseline before centrifugation. The ability of action of PRP is due to the range of GFs, cytokines, chemokines plasma proteins along with high range of platelet and complement of clotting factors. In addition to high platelet levels, PRP requires consideration of other parameters such as the appearance of white blood cells and activation. It defines the type of PRP used in various pathologies. PRP preparation is made easier by a variety of commercially accessible instruments. The makers claim that PRP devices often obtain a PRP concentration that is 2–5 times higher than the baseline concentration. Based on the white blood cell and fibrin content, the production of platelet-rich plasma can be divided into four majors.

Categories

LEUKOCYTE-RICH PRP (L-PRP). WBC Reduced PRP (P-PRP); Leukocyte Platelet Rich Fibrin and Pure Platelet Rich Fibrin. The rationale for the use of PRP in tissue repair is the efficiency of these specific growth factors. Addition of thrombin and calcium

chloride activates the collected platelets, thereby inducing the release of platelet growth factor, growth factor beta, fibroblast growth factor, insulin-like growth factors 1 and 2, vascular endothelial growth factor, Converts epidermal growth factor, interleukin-8, keratinocyte growth factor, binding tissue growth factor from alpha granules [9].

Method of Preparation

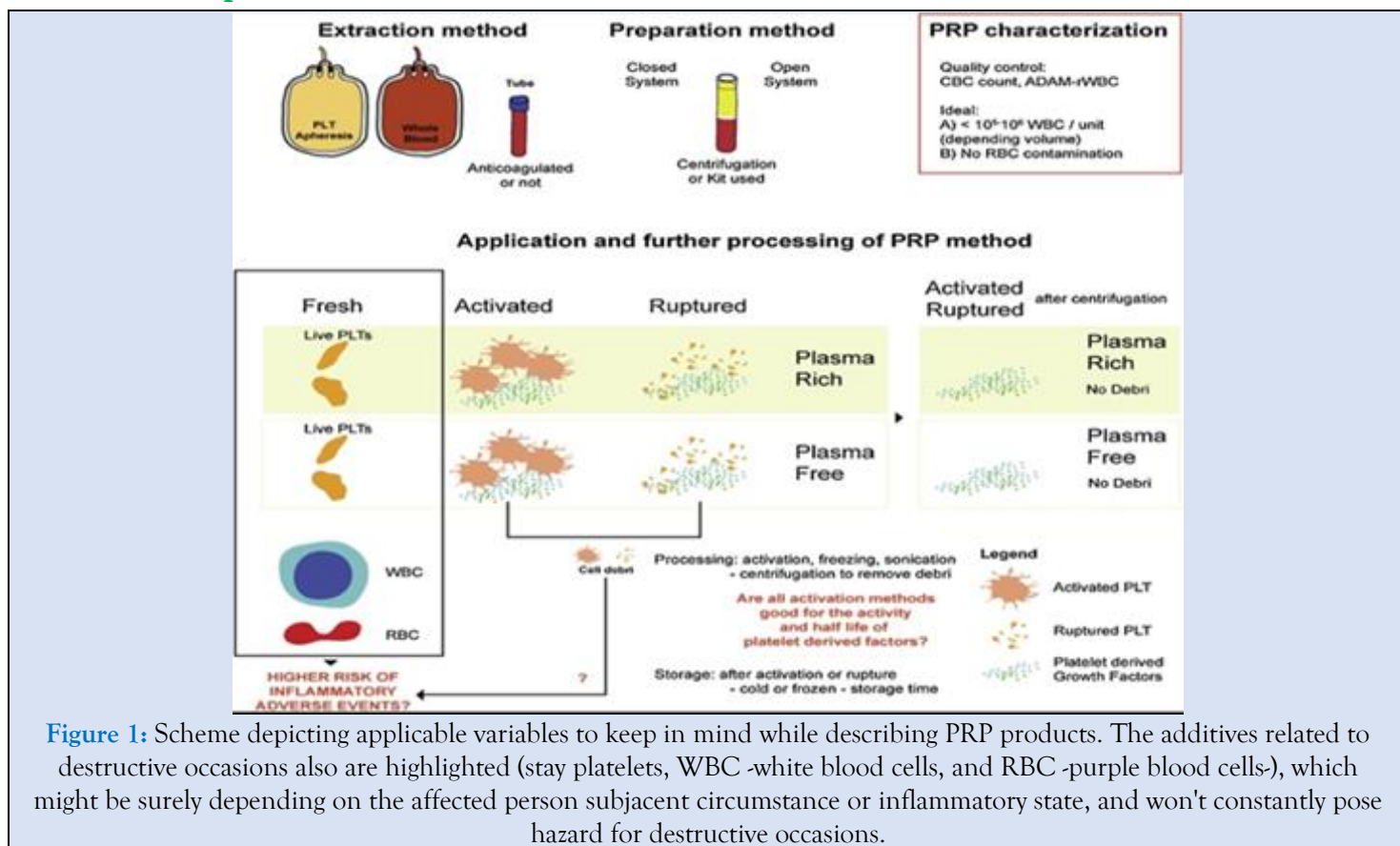


Figure 1: Scheme depicting applicable variables to keep in mind while describing PRP products. The additives related to destructive occasions also are highlighted (stay platelets, WBC -white blood cells, and RBC -purple blood cells-), which might be surely depending on the affected person subjacent circumstance or inflammatory state, and won't constantly pose hazard for destructive occasions.

Uses

With evidence of certain positive and negative effects, there is mixed evidence of benefit of PRP. It is shown to be tremendously effective in curing chronic tendinitis, osteoarthritis, and in Oral, faciomaxillary and plastic surgeries. Not only this but also according to a review in 2019, it is found useful in the rotator cuff disease. There is also evidence of its usefulness in osteoarthritis. Another meta-analysis made in 2019, found that in compared to hyaluronic acid, PRP is found more effective as an analgesic as well as improving function in osteoarthritis of knee [10]. Few randomized controlled trials in a review in the year 2009 evaluated that PRP was a definite promising treatment option for various orthopaedic illnesses such as treatment option for joints, ligament, tendon, muscle injuries such as lateral epicondylitis, muscle strain, Anterior cruciate ligament tears unless proven

otherwise.[11]. More recently there are evidence showing positive effects of PRP in promoting the endometrial and follicular growth factors not only this but also it is found assisting in gestation and reproductive cycles [12]. Due to the release of growth factors and biologically active protein there occurs a cascade of mechanisms stimulating neo angiogenesis and production of collagen. Hence due to this property it can be used for facial rejuvenation in the form of dermal injection and as a topical applicant in micro needling [13]. In a literature review done in 2015, PRP has shown positive results as a treatment option in Lymphedema. However, they suggest a deeper level of study to apply this in a large scale [14]. There is no evidence of effectiveness of PRP in conservative management in disease such as plantar fasciitis, Achilles' tendinopathy, based on a meta-analysis conducted in 2019. A Cochrane review in

2010 states that there is no clue of benefit in use of sinus lifts during dental implant placement. [15]. Keeping all these clinical uses aside, PRP has also been utilized greatly by the bio technicians in various tissue engineering applications in reference to bone, cartilage, akin and soft tissue repair. It has been serving as a source for delivery of growth factors or cells along with tissue engineered construction including bio materials.

Review

In several surgical specialities, Platelet-rich-plasma is an idiosyncratic substance that is frequently brought in use. Safety (because it is autologous material), enhanced platelet and growth factor deposition in the healing region, and quick preparation time are only a few of its many benefits.

There is a slow development of research in PRP used in OTOLARYNGOLOGY, but it is surely easier to find. 10 years from now, a very renown clinical Practitioner attended a lecture on topical applications of PRP after ablative laser procedures. It was found that his patients had a lot of pain and needed a lot of

time for healing. Surprisingly, with the application of PRP, they experienced less pain and improvement in healing time. He concluded that there were mostly opinion papers and non-randomized controlled trials then but now there is a broad spectrum of evidence on use of PRP in OTOLARYNGOLOGY and maxillofacial surgeries. It's property of wound healing is the strongest evidence of its use. Dual speed centrifugation is the principal method of production of Platelet-rich plasma. The equipment needed for blood centrifugation is shown in Figure 2a. There are two steps in the centrifugation. The first spin is a soft spin wherein blood is separates into red blood cells, platelet that is poor in plasma and a buffy coat. The second spin is termed as the hard spin where separation of platelet-rich plasma from the platelet poor plasma. The different layers produced by blood centrifugation is shown in figure 2b. After these two steps of centrifugation, the platelet-rich plasma which was extracted after the spin is mixed with Calcium chloride and thrombin and there is formation of a gel like product. This product is 5-8% concentrated than the whole blood [16].

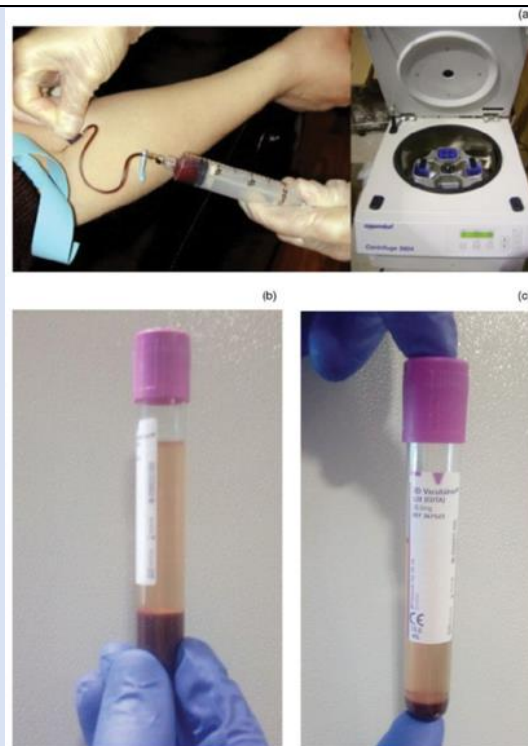


Figure 1

In addition to highly concentrated platelets, platelet-rich plasma contains a variety of growth factors beneficial for wound healing, including platelet-derived growth factor (PDGF), metabolic growth factor, and platelet-derived growth factor. Factors

such as beta ($TGF-\beta$), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor, platelet-derived angiogenesis factor, as well as leukocytes, phagocytes, and high-concentration natural fibrinogen. In particular, PDGF and TNF

promote haemostasis, scar reduction and faster wound healing. Platelet-rich plasma is an established

treatment with promising results for a variety of medical conditions [17].

Table 1: Platelet Growth Factor and Their Specific Characteristics.

Platelet Growth Factor Type	Growth factor Source	Biological Actions
Platelet derived growth factor (a-b)	Platelets, osteoblasts, endothelial cells, macrophages, monocytes, smooth muscle cells	Mitogenic for mesenchymal cells and osteoblasts, stimulates chemotaxis and mitogenesis in fibroblast/glia/smooth muscle cells, regulates collagenase secretion and collagen synthesis, stimulate macrophage and neutrophil chemotaxis
Transforming growth factor TGF(alpha-beta)	Platelets, extracellular matrix of bone, cartilage matrix, activated TH1 cells and natural killer cells, macrophages/monocytes and neutrophils	Stimulates undifferentiated mesenchymal cell proliferation; regulates endothelial, fibroblastic and osteoblastic mitogenesis; regulates collagen synthesis and collagenase secretion, regulates mitogenic effects of growth factors, stimulate endothelial chemotaxis and angiogenesis, inhibits macrophage and lymphocyte proliferation
Vascular endothelial growth factor, VEGF	Platelets, endothelial cells	Increases angiogenesis and vessel permeability, stimulates mitogenesis for endothelial cells
Epidermal growth factor, EGF	Platelets, macrophages, monocytes	Stimulates endothelial chemotaxis / angiogenesis, regulates collagenase secretion, stimulates epithelial /mesenchymal mitogenesis
Fibroblast growth factor, FGF	Platelets, macrophages, mesenchymal cells, chondrocytes, osteoblasts	Promotes growth and differentiation of chondrocytes and osteoblasts, mitogenic for mesenchymal cells, chondrocytes and osteoblasts
Connective tissue growth factor CTGF	Platelets through endocytosis from extracellular environment in bone marrow	Promotes angiogenesis, cartilage regeneration, fibrosis and platelet adhesion
Insulin like growth factor – 1 IGF -1	Plasma, epithelial cells, endothelial cells, fibroblasts, smooth muscle cells, osteoblasts, bone matrix	Chemotaxis for fibroblasts and stimulates protein synthesis. enhances bone formation by proliferation and differentiation of osteoblasts

The healing capabilities of this substance make it particularly intriguing to ENT surgeons as a potential filling or grafting material. Plasma rich fibrin (PRF) is considered satisfactory in wound healing. PRF can increase the closure rate of acute perforations, enhance the survival rate of autografts in TM surgeries and reduce the incidence of infections. According to a case report in 2019, the introduction of platelet-rich plasma in treatment of Sensorineural hearing loss along with steroids and antioxidants is doing revolutionary wonder. Its application in ENT is not yet widespread, thus more research is necessary. The data on Using platelet-rich plasma in ENT surgery is discussed in this review.

Materials And Methods

A search was undertaken on the present and potential uses of platelet-rich plasma utilizing different publications linked to otolaryngology. It was conducted using the PubMed database. One such instance is a randomized controlled trial with 76 patients as the sample size. All patients diagnosed with persistent suppurative otitis media and under the age of 55 were scheduled for myringoplasty. By using block randomization, the individuals were divided into two groups at random (block of 4). Group II

(n=38) was chosen as the control group and got saline-soaked gel foam intraoperatively. At the conclusion of the first and third months, a blinded examiner evaluated both groups. Group I (n=38) received platelet-rich plasma-soaked gel foam [18]. Another study was conducted on a group of 30 patients who had bilateral, generally symmetrical chronic rhinosinusitis that was unresponsive to any of the conservative management i.e., Medical treatment and would make them candidates for endoscopic sinus surgery. Patients with asymmetric disease or any additional confounding conditions were not taken into account. The procedure for the operation was followed as normal. In order to allow each patient to act as their own control, PRP was injected into the middle meatus on one randomly chosen side following each treatment while the other side was treated normally [19]. A case series study in 2018 was carried out in the ENT department of Harsh hospital itself in Ghaziabad. The participants were the patients with reduced hearing loss and had complications of fullness of ear. They were evaluated with the essential investigation such as PTA, BERA. On the basis of audiogram, 200 patients were recognized having pure sensorineural and mixed hearing loss. Over a period of 1 year, study over 200 patients were covered. 0.5 ml injection of PRP were injected intratympanic ally in

those 200 patients and it was repeated every 3 weeks along with comparative study of the audiogram with the previous preliminary audiograms. Among the 200 patients it was found that 172 had improvement in hearing after around five doses of the PRP injection. Although remaining 28 did not showed any improvement in hearing particularly. It should also be taken into account that all of them were above 70 years of age and 19 patients among them had diabetes as a predisposing factor [20]. In the year 2020, the year of COVID 19, another study was conducted in patients having olfactory loss of a duration more than 6 months with no evidence of sin nasal inflammatory disease and no history of improvement with olfactory training or topical agents. These patients were injected with intranasal PRP injection into the mucosa of olfactory cleft. The Sniff sticks olfactory test was conducted and observations were analysed up to 3 months. The results were quite impressive with improvement in symptoms [21]. On a study on osteonecrosis of the jaw which was mainly Related to Bisphosphonate commonly known as BRONJ. It was a case controlled randomized study in a group of 72 patients, all their treatment, surgical or non-surgical therapy was amplified by PRP gel for the observation of its effectiveness in osteonecrosis of Jaw. Due to its great wound healing capability, PRP showed amazing results. It's provided definitive evidence in its wound healing properties [22]. According to research on the use of PRP in ENT Surgical procedures, it is particularly effective in myringoplasty. A retrospective study demonstrated that combining PRP with fat graft myringoplasty (FMG) improved the closure of tympanic membrane perforations compared to FMG alone. Additionally, topical autologous PRP treatment is safe, highly effective, and successful during myringoplasty, with no documented complications. PRP helps chronic TM perforations heal more quickly, but it also prevents infection and eliminates the need for an inner EAC pack [23]. The data extraction consists of a narrative overview of each article due to the wide variation of study methodology and result.

Result

After obtaining the full Articles, their relevance and abstracts were evaluated for the final result that could conclude the potential of PRP.

Use of platelet-rich plasma in otology surgery

Following bilateral tympanic membrane puncture in 44 rats, Arklie et al. reported in 2009 that platelet-rich plasma helped the membranes repair [24]. Navarrete lark et al. reported the preliminary outcomes of type I tympanoplasty supported by platelet-rich plasma for central perforations in 2001. After placing a platelet-rich plasma plug around three patients' dry perforations, they underwent overlay type I tympanoplasty [25]. In 2013, Gopalkrishnan et al. took into account the examination of 25 patients who went underlay tympanoplasty with the use of PRP and another control group of 25 patients who had tympanoplasty without PRP. The rates of closure of the perforation were 96% in the experimental group and 80% in the control group [26]. Cho et al. In the year 2010, inspected the effect of Platelet-rich_plasma on the regeneration of ninth cranial nerve I.e., Facial nerve in 24 guinea Pigs. The group having Perineural microculture plus PRP and mesenchymal stem cells showed maximum myelinated axon Fibre group than the other ones [27].

Use of platelet-rich plasma in rhinology surgery

In order to cure atrophic rhinitis, Fiji et al. published a technique in 2014. They used autologous fat and platelet-rich plasma transplantation [28]. Pomerantz and Dutton in the year 2005 created a questionnaire series and compared the results with the control group in order to assess the lifestyle of 16- patients of all age group who underwent packing or filling with Platelet-rich plasma after the Endoscopic Sinus Surgery. Undoubtedly The PRP group outperformed the control group in terms of scores [29]. In 2006, Rice reported the same findings as Pomerantz and Dutton, he reported with the preliminary findings which were so impressive that strengthen the use of PRP in Ear packs. Following submucosal diathermy, Hussein and Salaheddin treated a herd of 30 patients in 2012 by injecting platelet-rich plasma into the inferior turbinate of the ear [30].

Use of platelet-rich plasma in laryngology surgery

Woo et al. (2014) examined the palliative effects of Platelet-rich plasma in Rabbits. They found that platelet-rich plasma appeared to preserve the wounded vocal fold's structure while reducing the production of granulation tissue [31]. In 2015, Cowden et al. Used various components of PRP such

as EGF receptor, FGF, Fibroblast GF Receptor 1 etc in repairing the Vocal cord and they were found very effective in healing of the Vocal Fold Scar [32].

TABLE II SIGNIFICANT FINDINGS IN STUDIES REVIEW, BROKEN DOWN BY SUBSPECIALTY	
Study	Conclusions
Otology	
– Gopalakrishnan <i>et al.</i> ¹	Improved healing times after underlay type I tympanoplasty; reduced graft displacement
– Erkilet <i>et al.</i> ⁶	Significantly improved tympanic membrane perforation healing time after PRP application
– Cho <i>et al.</i> ⁷	Combined use of PRP and MSCs improved facial nerve regeneration
– Navarrete Álvaro <i>et al.</i> ⁸	Overlay tympanoplasty type I outcome improved by PRP use
Rhinology	
– Pomerantz <i>et al.</i> ³	Packing with PRP after endoscopic sinus surgery improved patient quality of life
– Rice ⁴	No benefit of PRP as a packing material; study not completed
– Salaheldin <i>et al.</i> ⁹	Less crusting, less bleeding, improved mucociliary clearance with PRP injection after submucosal diathermy of turbinates
– Friji <i>et al.</i> ¹⁰	Autologous lipoaspirate plus PRP shortened mucociliary clearance time, reduced crusting and improved the appearance of nasal mucosa in atrophic rhinitis patients
Laryngology	
– Woo <i>et al.</i> ¹¹	PRP injected into injured vocal folds helped maintain their structure and decreased granulation tissue
– Cobden <i>et al.</i> ¹²	PRP applied to injured vocal folds increased the expression of growth factors, mainly EFGR and FGFR1
Paediatric ENT	
– Sidman <i>et al.</i> ⁵	No significant improvement in pain and recovery after tonsillectomy with PRP application
PRP = platelet-rich plasma; MSC = mesenchymal stem cell; EGFR = epidermal growth factor receptor; FGFR1 = fibroblast growth factor receptor 1	

Use of platelet-rich plasma in not surgery

The results of tonsillectomy following the application of platelet-rich plasma to the tonsillar fossae were reported by Sidman *et al.* in 2008. No discernible alterations were found [33]. The conclusion of each study is summarised in table 2 [34].

Conclusion

The numerous types of studies of the platelet rich plasma in Ear Nose Throat commonly known as otolaryngology surgery. When compared to the enormous uses of this significant material, the number of studies will always be 'Not Enough'. Every single article mentioned in the above had different experimental and control groups, each sharing some similarities as well in the methods of techniques and evaluation. It cannot be precisely concluded, with the broad-spectrum uses of platelet-rich plasma how much

essential is the wield of Platelet-rich plasma in the surgery of Ear Nose Throat Surgeries as some of the drawbacks included limitations in the aggregation participants and remissness to nurture a close delving up or some errors in the study design. Undoubtedly, Platelet-rich plasma is a boon for modern medicine with enormous potential clinical applications. The mechanism by which it aids healing process, by the promotion of growth factors aggregation is included in this review. The various surgeries of Otology, rhinology and laryngology and its effectiveness in various processes during the entire surgery, is compiled in this review. "Sometimes you have to go far to find what is close." For platelet-rich plasma (PRP) as we currently understand it, Paulo Coelho's adage still holds true. Although much progress has been made in our knowledge of this "Youth" in blood, there still appears to be much to learn. Despite advancements, understanding on its preparation,

biology, and end product's qualities continues to elude scientists.

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