

Placenta Extract -the Magical wound Healer, Next Milestone in the Healing of Periodontal Surgery

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Abstract: Traditional folk medicine is the basis of Indian Ayurveda without any ill effects , Right from the days of Sushruta in Ancient India, due to various battles and wars, healing of wounds was a matter of attraction for all including ancient Chinese, Korean, Egyptian and African healers. Sushruta Samhita describes dealing with healing of these wounds, and describes more than 100 plants & vital fluid for treatment of wounds .In 21st century while we still can't perform miracles in healing to maintain health ,one Elixir is coming into the limelight is Placenta Extract which will aid magic in the era of wound healing.In other words ,the Placenta act as various internal organs for the embryo, that's why it has a various medicinal effects ,In this review we are documenting magical effects of wound healing .

Keywords: Placenta extract; wound healing

I. Introduction

The wound is defined as, A forced separation or circumscribed damage of skin or mucosa, The history of wound care spans from prehistory to new era of medicine. Wounds naturally heal by themselves, but hunter-gatherers would have noticed several factors and certain herbal remedies would speed up or assist the process, especially if it was grievous.

Right from the days of Sushruta in Ancient India, due to frequent battles and wars, healing of wounds was a matter of concern for all including ancient Chinese, Korean, Egyptian and African healers. Sushruta Samhita has two separate chapters dealing with healing of these wounds, and describes more than 100 plants for treatment of wounds both singly and in combination.

In ancient history, this was followed by the realization of the necessity of hygiene and where wound dressing techniques and surgery developed, Over time, different civilizations began to create their own herbal medicinal treatments for wounds depending on the trees, shrubs, or any other type of animal derived fluid located in their environment. These herbal treatments became the oldest form of wound therapy, Numerous ancient herbal remedies and poisons now serve as models for modern medicine. For example, curare, which was an ancient South American arrow poison, was used in the 20th century as the muscle relaxant tubocurarine.

The earliest known to men is the Rhizotomika of Diocles of Carustius, a student of Greek philosopher Aristotle. This book includes the author's observation of the effects of the herbal medicine on specific parts of the human body. This then became the beginning of scientific research on herbal remedies on humans, which has been modified and significantly changed from modern wound remedies .The Greeks also acknowledged the importance of wound closure, and were the first to differentiate between acute and chronic wounds, calling them "fresh" and "non-healing", respectively.

The clinical history of the treatment of acute and chronic wounds can also trace its origins to ancient Egypt. The Ebers Papyrus, circa 1500 BC, details the use of lint, animal grease, and honey as topical treatments for wounds. The lint provided its natural absorbency, the animal grease provided a barrier to environmental pathogens, and the honey served as an antibiotic agent.

He first advances in wound care in this era began with the work of Ignaz Philipp Semmelweis, a Hungarian obstetrician who discovered how hand washing and cleanliness in general in medical procedures prevents maternal deaths .

Use of placenta as a therapeutic agent has been prevalent for a long time. It is an immunologically privileged organ and has unique pharmacological effects like enhancement of wound-healing, anti-inflammatory action, analgesic effect etc. A variety of substances with biological and therapeutic activity present in human placenta, have been isolated and identified as hormones, proteins, glycosaminoglycans, nucleic acids, polydeoxyribonucleotides (PDRNs) etc. The composition of placental extract thus depends on the method of its

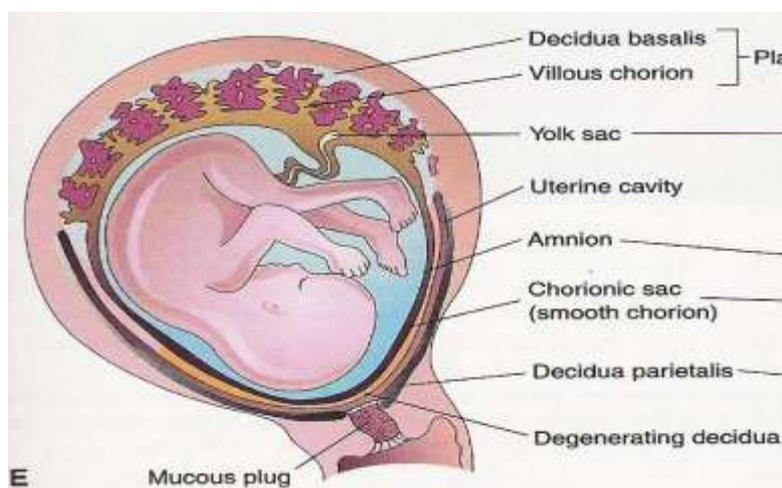
preparation. Consequently, it shows different therapeutic activities. In many countries, intra-muscular and topical use of the extract for burn injuries, chronic wounds and as postsurgical dressing is an age-old practice. Under such conditions, an effective tissue-regenerative agent needs to take care of prevention of secondary bacterial or fungal infection. Recently, presence of biologically active NADPH and fibronectin type III like peptide in the extract has been demonstrated. Further, different spectroscopic and chromatographic analyses have revealed high degree of consistency among different batches of the extract.²

Another form of attack the placenta uses is its various growth abilities, such as the ability to accelerate growth of the liver, as observed in the re-growth of cells and organs. This liver regenerative effect alone has been shown in animal testing to be effective for almost all diseases other than cancer, such as hepatitis, cirrhosis of the liver, heart disease, stroke, and renal failure. the placenta is now viewed by many as a substance which will revolutionise modern medicine.

Homeostasis works to create a balance between the nervous system, hormonal system and immunological system the Placenta increase the healing by stimulating the nervous regulation, hormonal regulation, & immune system regulation and gives resistance to the body. We often hear that modern disease is caused by free radicals, Placental extract removes the free radicals strengthen the human body, in addition Placental extract acts to improve basic metabolism, strengthen the liver & counter toxin, counter inflammation, accelerate the recovery of wound, promote circulation however no much documentation is present over the placental extract, this review explore the magical properties of mother's fluid so that it can be used for mankind purposes.

Structure Of Placenta

Placenta is a maternofetal organ which is the primary site of nutrient and gas exchange between the fetus and the mother. Human Placenta is discoidal, haemochorial, chorioallantoic and decidual. Is a union between developmental adenexa (extra-embryonic membranes and the uterine mucosa) for physiological exchange.³



Placenta has two components –

A fetal part that develops from the chorionic sac.

A maternal part that is derived from the endometrium.

By the beginning of the fourth month, the placenta has two components:

(a) a fetal portion, formed by the chorion frondosum

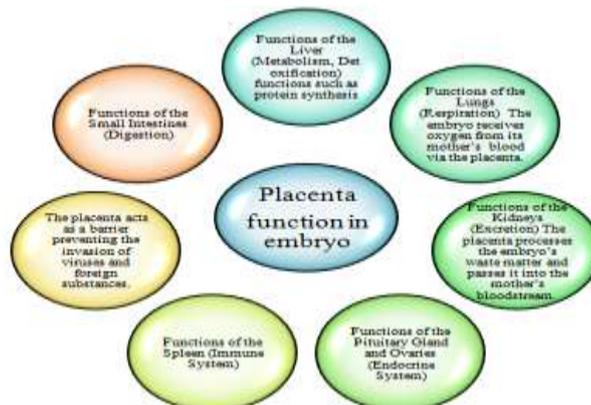
(b) a maternal portion, formed by the decidua basalis.

On the fetal side, the placenta is bordered by the chorionic plate, On the maternal side, the placenta is bordered the decidual plate. The fetal surface of the placenta (facing the fetus) has a shiny, smooth surface provided by the amniotic membrane that covers it. A number of large arteries and veins, the chorionic vessels, converge toward the umbilical cord. The attachment of the umbilical cord is usually eccentric and occasionally even marginal. Rarely, however, does it insert into the chorionic membranes outside the placenta (velamentous insertion). Maternal side of the placenta is textured and spongy looking. It is divided by a series of fissures into lobules or cotyledons. The fissures contain the remains of septae which extended between the maternal and fetal portions. The placenta begins to form in around the fifth week after conception, and fully grown by the 13th week.

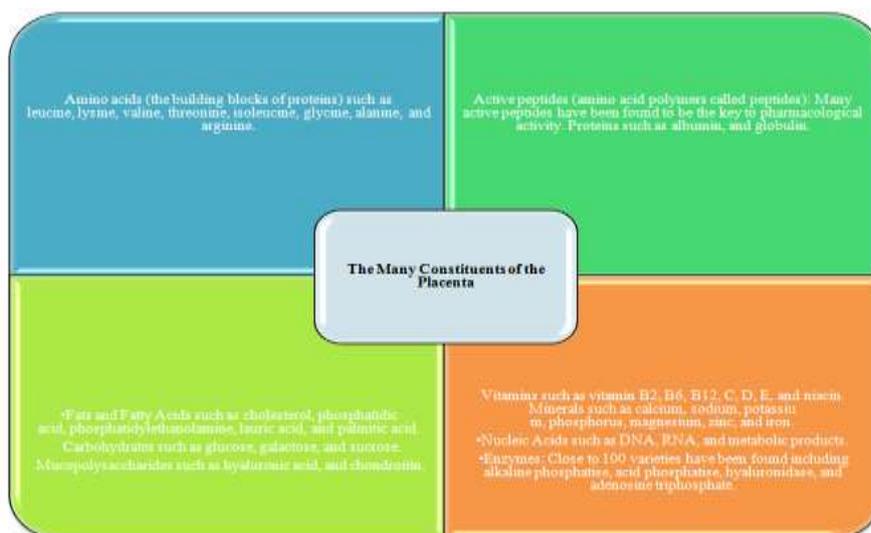
Main functions of the placenta are (a) exchange of metabolic and gaseous products between maternal and fetal bloodstreams and (b) production of hormones .⁴

The Placenta Acts as a Substitute for an Embryo's Organs

The functions performed by the placenta in place of organs can be summarised as follows.



As we can see, the placenta acts as an agent for various organs for the undeveloped embryo. we might call it an all-purpose organ.



Growth Factors will revolutionise 21st Century Medicine

Main Growth Factors of the Placenta

- Hepatocyte Growth Factor (HGF): Promotes growth of liver parenchymal cells and various tissues.
- Nerve Growth Factor (NGF): Promotes growth of nerve cells (sensory and sympathetic ganglionic cells).
- Epidermal Growth Factor (EGF): Promotes growth of skin, lungs, cornea, and tracheal epithelial cells.
- Fibroblast Growth Factor (FGF): Promotes growth of human fibroblasts, glia cells, and vascular endothelial cells.
- Insulin-like Growth Factor (IGF): Promotes growth of cartilage cells, and smooth muscle cells.
- Colony-Stimulating Factor (CSF): Promotes growth of stem cells such as immuno-competent cell granulocytes, and macrophages.
- Interleukin-1 (IL-1): Promotes production of immune-competent cells (T-cells, B-cells, and NK-cells), thymus cells, and lymphokines.
- Interleukin-2 (IL-2): Promotes growth of T-cells (helper T-cells, killer T-cells, and suppressor T-cells).
- Interleukin-3 (IL-3): Promotes growth of hematopoietic cells, and mast cells.
- Interleukin-4 (IL-4): Promotes growth of B-cells, and promotes division of antibody-producing cells.

Is Placenta Extract Old Or New Herbal Remedy

The placenta has a history of medicinal use starting more than 2000 years ago. It was used as an **nector** of eternal youth during the Qin Dynasty in China (259 BC to 210 BC). It appears in a medical text authored “Honzo Syui” from the Tang Dynasty (618 AD to 907 AD) under the names “Jinho” or “Hoi”. It appears again in the Ming Dynasty (1368 to 1644) as “Shikasha” in the book “Bencao Gangmu”, where it is prized as nourishing magical herbal remedy for physical and mental tiredness and weakness. In Taoism, the elixir used to become a wizard is called “Kasha”. Yang Kwei-Fei is said to have often prescribed “Shikasha”.

In modern times too, it is an important ingredient in Kampo medicine. “Shikasha” also appears in a Korean medical text entitled “Dongui Bogam” (1613). In the Edo Period in Japan (1603 to 1868) the same “Shikasha” was one of the three main active agents in a treatment called Kongentan from the town of Kaga in the modern Ishikawa Prefecture. Also in the West, Hippocrates, a doctor in Ancient Greece called “the father of Western medicine”, used placenta in his treatments. Cleopatra also said to have used placenta for rejuvenation and beauty.

But somehow, while the use of placenta as a traditional medicine has persisted in the East, it has been forgotten in the West since the time of the Middle Ages, and it wasn’t until research was done in the 1930s in the Soviet Union that the placenta’s usefulness once again saw the light of day.

Research on human placental extract gained a velocity with the description of the preparation of its extract by Russian ophthalmologist Prof. V.P. Filatov. Professor Filatov was a medical school professor in Odessa in the Soviet Union. Recent medical history from 1912 showed that Filatov started research on grafting human. He observed that when animal or vegetable tissues are isolated from the organism and subjected to the action of environmental factors that inhibit their vital processes, they undergo a biochemical homeostasis. In consequence to this readjustment, the tissues develop substances that stimulate their vital processes. Filatov named these substances as *Biogenic stimulators* (Filatov, 1951). After many clinical experiments, Filatov was convinced that any tissue of human or animal origin could be used to obtain curative effect. He applied this principle to general medicine and confirmed that the process was just as valid for other human tissues. That is how the principle of therapeutic tissue was originated. Prof. Filatov reported that “the Placenta not only activates the functions of the whole body, it is also excellent at promoting recovery of diseased areas”. In 1945, Prof. Filatov was awarded the highly influential Lenin Prize for his superb achievements⁵.

Shortly afterwards, “Tissue Therapy” came to Japan. In 1950, a group of physicians researching “Tissue Therapy” got together and established the “Tissue Therapy Research Institute”. After developing Placenta Extract injections, in 1956 they founded “Melsmon Pharmaceutical Company Limited” which quickly obtained government approval, and began manufacture and sale of Melsmon injections as a treatment for menopausal disorders and failed lactation. Later, in 1959, Placenta Extract injections based on Prof. Hieda’s research came to market under the name “Laennec” at that time approval was given from the Japanese government for use in the treatment of hepatitis

In Korea, HPE has been approved for the improvement of liver function and menopausal symptoms since its importation from Japan in 2003. In Korea, HPE has been approved and is now widely used for improvement of fatigue, skin whitening, and antiaging. Despite this popularity, the efficacy of HPE has not been sufficiently researched.

Preparations of human placental extract

Placental extracts can be classified into two different types:

- aqueous extract
- hydroalcoholic extract.

The components present in the extract depend on the method of its preparation and are based on solubility of the components in respective solvent of extraction. Thus, an aqueous extract is likely to contain more polar molecules such as peptides/proteins, small organic components like amino acids, nucleotides, polydeoxyribonucleotides (PDRNs), carbohydrates and trace amount of lipids mostly bound to proteins which are comparatively soluble in aqueous medium. Likewise, various types of lipids may be present in hydroalcoholic extract (less polar and hydrophobic). Chemical analysis of the hydroalcoholic extract revealed the presence of glycosphingolipids, cholesterol, triglycerides, high density lipoproteins, carbohydrates, sialic acids and others, including amino acids, nucleotides, carotenes, vitamins, including small amount of low-molecular-weight proteins/peptides containing hydrophobic amino acid residues which are soluble in a less polar solvent.

Modern indigenous aqueous placental extract is prepared employing Filatov’s procedure.

As follows:

fresh placentae were stored in ice and portions were tested for HIV antibody and Hepatitis B surface antigen. Single hot and cold aqueous extractions were done after incubating dissected and minced placenta at 90°C and 60°C respectively. This was followed by sterilization of the extract under saturated steam (pressure 15-lbs/sq inch at 120°C for 40 min). After filtration and addition of 1.5% (v/v) benzyl alcohol as preservative, ampoules were filled and sterilized once again under the said condition for 20 min. This is apart from adding safety margins to the temperature, time or both to destroy most resistant spore-producing species like *Clostridium tetani*. The terminal sterilization step was to maintain sterility of the products after they were filled and sealed in ampoules. Each milliliter of the drug was derived from 0.1 g of fresh placenta. The trade name of the extract is 'Placentex'. Carried over bioactive components in the extract depends on the method of its preparation.⁵

Mechanism of Role of Placental extract in wound healing

Wound healing is a very complex process that includes inflammation, cell migration, extracellular matrix deposition and cell maturation. Several cytokines and growth factors are involved in inducing different cell types for healing.

Among all the extracts of placenta that have been prepared, only the aqueous extract has been shown to have potent clinical efficacy in terms of healing. Aqueous extract from placenta is used as a licensed drug for wound healing under different trade names in India. This could be due the fact that the aqueous extract is a rich source of various bioactive peptides with tissue regeneration potential. In addition, the extract also retains amino acids, nucleotides, polydeoxyribonucleotides and carbohydrates that might be responsible for wound healing. Placental extract plays a beneficial role as a topical agent in the management of chronic non-healing wounds.



Mechanism proposed are :

1. NADH and NADPH. These are natural constituents of placenta and play important roles in different metabolic pathways including wound healing , Since NADPH is known to regulate a number of phenomena related to wound healing,. Biological functionality of the fluorophore in the extract has been confirmed by enzymatic assay. It has been shown that NADPH in aging human skin cells increases synthesis of collagen involving filaggrin and keratin *in vitro*
2. It has been well documented that nitric oxide (NO) has multiple effects at the molecular, cellular and physiological level in wound healing. It promotes inflammatory mediation of repair mechanism and wound matrix development followed by remodeling. NO mediated cellular signaling possibly enhances wound repair by increasing tissue oxygen availability through angiogenesis , The extract also has the ability for *in vitro* NO induction in mouse peritoneal macrophage and human peripheral blood mononuclear cells (PBMC).
3. The extract has also shown to induce interferon- γ (IFN-production by macrophages Considering the importance of peptides in wound healing.
4. Primary investigation revealed that the drug stabilizes some serine proteases against their autodigestion by reversibly inactivating them, which enhances the efficiency of proteolytic enzymes thereby facilitates wound healing.⁵ The component responsible for the proteolytic activity was identified to be an ubiquitin-like protein It is already known that ubiquitin and ubiquitin-like proteins (Ubls), collectively known as ‘ubiquitons’, perform a host of important functions such as protein degradation, antigen processing, apoptosis, biogenesis of organelles, cell cycle and division, fertilization and gametogenesis, DNA transcription and repair, differentiation and development, signaling, immune response and repair.
5. Further it has been demonstrated that one or more peptides from human placental extract including fibronectin type III stabilize trypsin activity after strong association, which is reversible in nature. Trypsin and similar proteolytic enzymes help in debridement and prevent keloid formation during wound healing and therefore regulation of its activity is an important criterion⁵

Other Therapeutic Effects Of Placental Extract

Placenta Can Treat the Following Conditions

- Gynaecology: menopausal disorders, menstrual pain, irregular menstruation, failure of lactation, and high prolactin levels, etc.
- Internal Medicine: hepatitis, cirrhosis of the liver, chronic pancreatitis, diabetes, chronic gastritis, dyspepsia, gastric ulcers, duodenal ulcer, ulcerative colitis, bronchial asthma, chronic bronchitis, high blood pressure, low blood pressure, habitual constipation, and collagen disease,
- Surgery: chronic rheumatoid arthritis, osteoarthritis, arthritis, neuralgia, lumbago, and stiff shoulders, etc.
- Dermatology: atopic skin complaints, psoriasis, body odour, eczema, chapped skin, spots, and freckles, etc.
- Psychiatry: autonomic ataxia, and sleeplessness, etc.
- Urology: enlarged prostate, cystitis, and haemorrhoids, etc.
- Ophthalmology: cataracts, allergic conjunctivitis, and vision loss, etc.
- Ear, Nose and Throat: allergic rhinitis, Meniere's disease, and hay fever, etc.
- Dentistry: Periodontitis, and gum disease, etc.

II. Conclusion

Natural medicine continues to play an important role for prevention, alleviation and cure of diseases. In some part of the Western world, the use of traditional medicine has been largely lost. However, it is a widespread phenomenon in the developing countries where 80% of the population is still relying on traditional medicine for primary healthcare. Derived from folklore, human placental preparations show immense therapeutic value and can be safely used once it is ensured that the source is free from fatal infections like HIV, HBV, HCV and alike. The aqueous extract of human placenta is a scientifically proven potent wound healer. Characterization of active components present in different placental preparations and correlating them with their therapeutic actions are the promising avenue for future study. Identification of other biologically active components in the extract and their mechanism of action in terms of cellular signaling, which play significant role in wound healing also needs to be addressed. We can make use of the amazing power of HGF, the Happy Growth Factor, right now by using Placenta.

References

- [1]. Concepts Of Healing In Periodontal Therapy - Part I Dr. Shubham Kumar1 , Dr. Krishna Kumar Gupta2 ,Dr. Devleena Bhowmick3 , Dr. Abhishek Singh4 Iosr Journal Of Dental And Medical Sciences (Iosr-Jdms) E-Issn: 2279-0853, P-Issn: 2279-0861. Volume 14, Issue 10 Ver. Xi (Oct. 2015),

- [2]. In Vitro Growth Inhibition Of Microbes By Human Placental Extract Piyali Datta Chakraborty And Debasish Bhattacharyya* Indian Institute Of Chemical Biology, 4, Raja S.C. Mallick Road, Jadavpur, Kolkata 700 032, Indiaceut Science, Vol. 88, No. 5, 10 March 2005
- [3]. Ubiquitin-Like Protein From Human Placental Extract Exhibits Collagenase Activity Debashree De1, Piyali Datta Chakraborty2, Jyotirmoy Mitra1, Kanika Sharma1, Somnath Mandal1, Aneeha Das1, Saikat Chakrabarti1, Debasish Bhattacharyy , Research And Development, Albert David Ltd., Calcutta, West Bengal, Indiaplos One | Wwww.Plosone.Orgmarch 2013 | Volume 8 | Issue 3
- [4]. Reduction Of Tumorigenicity By Placental Extracts Annette M. Marleau1, Greg Mcdonald2, James Koropatnick3,4, Chien-Shing Chen5 And David Koos6anticancer Research 32: 1153-1162 (2012)
- [5]. Aqueous Extract Of Human Placenta As A Therapeutic Agent Piyali Datta Chakraborty1 And Debasish Bhattacharyya2,* Ialbert David Ltd, Kolkata, Recent Advances In Research On The Human Placenta-Intech
- [6]. Craig Rp. The Quantitative Evaluation Of The Use Of Oral Proteolytic Enzymes In The Treatment Of Sprained Ankles. Injury 1975; 6: 313-316.
- [7]. Datta P, Bhattacharyya D. Spectroscopic And Chromatographic Evidences Of Nadph In Human Placental Extract Used As Wound Healer. J. Pharma. Biomed. Anal. 2004a; 34: 1091-1098.
- [8]. Datta P, Bhattacharyya D. Analysis Of Fluorescence Excitation-Emission Matrix Of Multicomponent Drugs: A Case Study With Human Placental Extract Used As Wound Healer. J. Pharma. Biomed. Anal. 2004b; 36: 211-218.
- [9]. De D, Chakraborty Pd, Bhattacharyya D. Analysis Of Free And Bound Nadph In Aqueous Extract Of Human Placenta Used As Wound Healer. J. Chromatogr. B. 2009; 877: 2435
- [10]. De D, Chakraborty Pd, Bhattacharyya D. Regulation Of Trypsin Activity By Peptide Fraction Of An Aqueous Extract Of Human Placenta Used As Wound Healer. J. Cell. Physiol. 2011; 226: 2033-2040.
- [11]. Diegelmann Rf, Evans Mc. Wound Healing: An Overview Of Acute, Fibrotic And Delaye Healing. Front. Biosci. 2004; 9:283-289.