



OMENTUM

Use of Omentum in Medicine and Surgery:
Current Therapy and Future Prospects

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1-800-645-5048
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Contents

Introduction	3
The Omentum	4
•Human anatomy	
•Physiology	
•Omentum-mediated angiogenesis	
Characteristics of porcine omentum and its affinity with human tissues	11
Omental lipids: chemical composition	12
Pharmacological properties of omentum	13
Use of autologous omentum in surgery	18
•omentum in experimental surgery	
•omentum in plastic and reconstructive surgery	
•omentum in neurosurgery	
Topical use of heterologous purified omental lipids	23
Local tolerability of heterologous purified omental lipids	35
Conclusions	37
Cabot P.O.L. Cream	40
Bibliography	31

Introduction

Introduction

The study of omentum and its therapeutic possibilities is in fact an “old” topic, but one which is now supported by modern scientific rationale.

The omentum:

1. the anatomical-physiological features which characterise omentum
2. chemical and molecular composition.
3. Studies (*in vitro* and *in vivo*) carried out with omentum in both medical and surgical disciplines.

It becomes clear that a topical preparation able to stimulate local microcirculation and skin regeneration can make an important contribution in situations where the dermo-epidermal barrier has lost, or is at risk of losing, its integrity and functionality.

Such a preparation, formulated to combine the characteristics of a good emollient with the skin-trophic advantages derived from the properties of purified omental lipids, can prove to be very useful to dermatologists in treating a wide variety of frequent skin conditions.

We believe that, upon reading the information presented in this volume, general practitioners and doctors of other specialisations will also be able to identify additional, and to some extent different, clinical situations where the use of products containing purified omental lipids can prove beneficial.

Nature has provided us with a useful and safe therapeutic tool which can be exploited in a variety of different clinical pathologies and conditions.

Omentum

Human anatomy

The peritoneum is the most extensive serosa in the human body. It is a thin, transparent membrane with a smooth surface which covers the organs found in the abdominal cavity and part of those in the pelvic cavity.

The omentum is a large peritoneal fold. It begins at the stomach and extends downwards to cover the abdominal organs. It serves a primarily protective role, especially in defending against infective agents. It is often compared to a closed sack which adheres on one side to the abdominal wall and on the other to the walls of various organs, thus forming the parietal and visceral layers respectively.

The omentum is a large peritoneal fold. It begins at the stomach and extends downwards to cover the abdominal organs. It serves a primarily protective role, especially in defending against infective agents

The two layers are attached to one another except in proximity to visceral walls and surfaces, where they separate to form the coating of the abdominal-pelvic cavity and individual organs. The visceral and parietal peritonea are connected by means of mesoes, ligaments and the omentum.

The mesoes, which like the ligaments extend from the walls to the viscera, have various names according to the organs they suspend (mesentery for the intestine, mesogastrium for the stomach, etc.). In addition to supporting the organs, they are also important for tissue trophism as they contain veins and nerves. Ligaments are primarily for anchoring.

The large omentum covers the loops of the small intestine, extending to the pubis. The omenta (or epiploon) are abdominal structures formed by the peritoneum which run between two or more viscera. The small omentum, divided into two portions (hepatoduodenal ligament and hepatogastric ligament), covers the hepatic lobe and extends from the first tract of the duodenum to the small

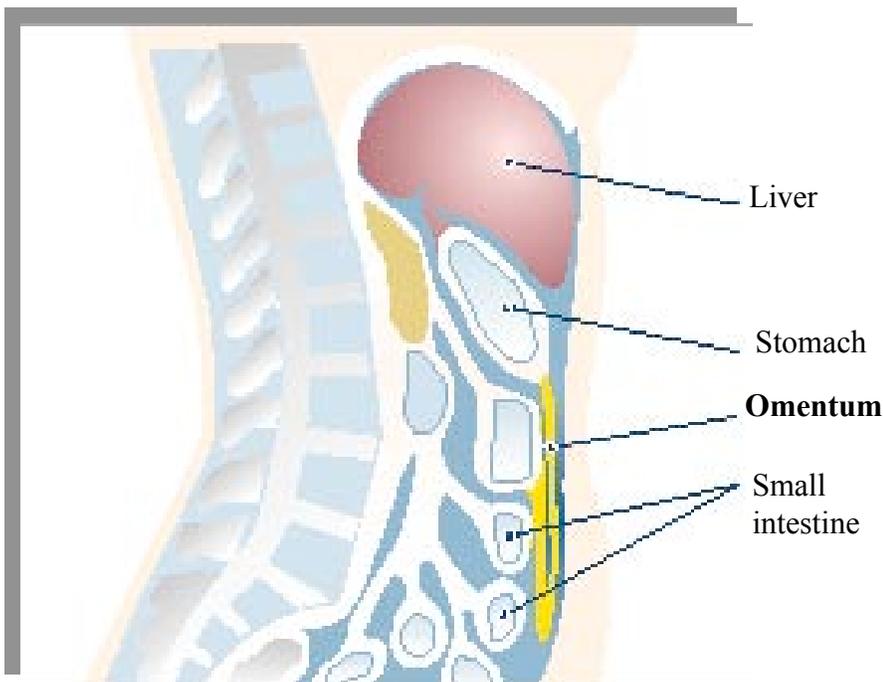
Omentum

curve of the stomach. The large omentum descends from the small intestine loops to almost the pubis, forming the gastrocolic ligament from the large gastric curve to the anterior face of the colon, and the omental apron in the remaining areas. The gastrocolic ligament is formed from two peritoneal layers which are the direct continuation of the peritoneum covering the stomach. Extending downwards, these two layers cover the small intestine before heading back upwards to the colon. The omental apron is thus formed from the coalescence of four layers¹ (Figure 1).

The large omentum covers the loops of the small intestine, extending to the pubis

The gastrocolic ligament and omental apron make up the large omentum. The small omentum is formed by the hepatoduodenal and hepatogastric ligaments.

Figure 1 – The human omentum: anatomy



Omentum

Physiology

One of the main roles of the peritoneum and thus the omentum is to defend the abdominopelvic viscera from various kinds of aggression, and in particular that of infective agents. In the presence of infective or inflammatory processes, the peritoneum tends to adhere to the affected area in an attempt to circumscribe the damage.

The peritoneum's function, and that of omentum, is essentially to protect intestinal organs from aggression

The peritoneum's function, and that of the omentum, is essentially to protect intestinal organs from aggression.

The importance of this protective and isolating function is obvious in such situations as ulcers, hernias, appendicitis and tumours. In fact, in such situations it has been observed that the omentum tends to surround the affected area in order to limit the risk of peritonitis as much as possible².

The omentum's defensive properties are due to its mobility and structure

Its defensive ability is due to its extreme mobility within the abdominal cavity and its anatomical structure: the entire peritoneum is covered by a microscopic mesothelium which rests on a lamina of its own, and often by a connective subserous tela. The large omentum is rich in fixed microphages which are mobilised during inflammatory processes.

The omentum's defensive properties are due to its mobility and structure.

Flowing between the layers is the peritoneal liquid made up of electrolytes, protein and other substances originating from the interstitial fluid and blood plasma. Various cell populations are also present depending on the various physiological and pathological conditions.

Omentum

This is not surprising given that the omentum's vascularisation is far in excess of its needs (the anterior lamina is supplied with blood by the right and left gastroepiploic arteries, the posterior lamina by the epiploic arteries) and therefore constitutes a potentially very active metabolic and immunological environment.

The omentum is characterised by extensive vascularisation, sign of a metabolically active environment.

In addition to its protective function and contribution to visceral mobility and equilibrium, the large omentum also contains a considerable quantity of adipose tissue; this despite its thin net structure (Figure 2). The lipids contained in this tissue carry out very important activities for the organism¹, and in particular the presence of neutral glycerides, phospholipids, glycolipids and gangliosides suggest the potential usefulness of heterologous omental lipid fractions in dermatology.

The large omentum is rich in lipids, and in particular, neutral glycerides, phospholipids, glycolipids and gangliosides.

Amongst the less immediately-obvious properties of omentum but, as we shall shortly see, one which has recently gained considerable therapeutic importance, is its ability to stimulate *in vivo* tissue neoangiogenic processes which are very much involved in reparative functions.

The omentum is characterised by extensive vascularisation, sign of a metabolically active environment

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Omentum

The omentum's angiogenic properties have been known for many years and it is routinely used in surgery to promote wound healing, keep circulation going in transplant organs and tissues, and provide a reservoir of vein and arterial vessels for skin grafting.

In addition to its protective functions, it appears that omentum has the ability to stimulate neoangiogenic processes

In addition to its protective functions, it appears that omentum has the ability to stimulate neoangiogenic processes.

The omentum's other functions involve its ability to produce trophic factors for various tissues. Amongst these are neurotrophic factors, a family of substances which promote neurone growth and regeneration, and factors which promote epithelial regeneration and thus stimulate the turnover of cells such as skin keratinocytes.

Figure 2 – The omentum's thin net structure



Omentum

Omentum-mediated angiogenesis

Early observations regarding the omentum's ability to stimulate vascular proliferation lead experimenters to hypothesise its use in therapies designed to regenerate tissue or prevent ischaemic conditions. The numerous trials carried out to this end *in vitro* and *in vivo* will be discussed in later chapters.

Given the importance of regulating angiogenic processes in a wide variety of physiological and pathological conditions, much interest was placed in understanding the mechanisms responsible for the omentum's positive contribution to wound healing and revascularisation of ischaemic tissue.

Amongst the various polypeptide growth factors with angiogenic activity present in the omentum is the VEGF (Vascular Endothelial Growth Factor)

Thirty years ago Goldsmith et al³ suggested the existence of a vascular-stimulating factor which appeared to be extracted along with the omentum's lipid component given that the lipid component reproduced the angiogenic properties of the entire omentum.

It was only recently, however, that the numerous polypeptide growth factors with angiogenic activity were discovered, and that they could be identified and detected in the omental tissue.

Administrations carried out in various rat tissues to measure the Vascular Endothelial Growth Factor (VEGF) demonstrated that the omentum is in fact the tissue with the highest concentration of VEGF.

Amongst the various polypeptide growth factors with angiogenic activity present in omentum is the VEGF (vascular endothelial growth factor)

Omentum

In the omentum, the VEGF is produced primarily by adipocytes

Molecular studies using Western and Northern blot techniques (measuring the presence of proteins and RNA respectively) were also carried out in conditions of both normal oxygenation and hypoxia in order to better characterise the presence of VEGF in omental tissues. The results demonstrated that the cells primarily involved in producing VEGF are the omentum's adipocytes and not the mesothelial or vessel stroma cells.

In the omentum, the VEGF is produced primarily by adipocytes.

It has also been found that the VEGF gene is continually transcribed in the adipocytes and thus constantly produced. Incubating these cells in hypoxic conditions, however, the protein's expressivity is 1.7 times higher than in normal oxygenation conditions and there is a similar increase in the quantity of mRNA in the cells.

These findings suggest that there is a transcriptional mechanism which regulates VEGF production and that stimulation is induced by a reduction in oxygen levels⁴.

These recent experimental data thus confirm earlier findings regarding the omentum's angiogenic activity in conditions of normal oxygenation, as well as its increased activity in conditions of hypoxia. At this stage, it appears very likely that the VEGF is the main factor responsible for the omentum's ability to stimulate vascular proliferation.

Characteristic of porcine omentum and its affinity with human tissues

When the potential of omental lipids was understood, the need to obtain large quantities of the tissue from a readily-available source for study and therapeutic use lead to the search for a suitable animal source. Pigs were immediately identified as the ideal source for a number of reasons.

Porcine tissue was in fact examined due to its ready availability and high angiogenic activity. By isolating the mesothelial cells of porcine omentum, it was also found that the phenotypic characteristics and functional properties were identical to those of human omentum⁵.

The compatibility of porcine tissues with those of humans is also evident with respect to the omentum: porcine omentum features the same phenotypic characteristics and functional properties as the human omentum.

It should also be remembered that tissues of porcine origin are often used in medicine due to their similar genetic properties with respect to those of humans: substitute heart valves, xenografts, genic therapy studies, and the widespread use of molecules of porcine origin (GH, insulin) before the advent of recombinant DNA technology.

Pigs are monogastric animals (i.e. non ruminating) and, in contrast to horses, have cholecysts: even from an anatomical perspective, their abdomen presents surprising similarities to that of humans. Lastly, in terms of safety, tissues of porcine origin have never been involved in problems regarding prions and the possible transmission of infections to humans.

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Omental lipids: chemical composition

Omental lipids: chemical composition

The experiments carried out on omentum have demonstrated that pure omental lipid extracts are able to completely reproduce the angiogenic activity of the entire organ.

The omentum's lipid component can be extracted using an organic solvent, or a mixture of organic solvents (e.g. hexane or methanol).

The lipid extract obtained from porcine omentum can be separated to facilitate identification of its main components⁶.

97% neutral triglycerides,
3% phospholipids, neutral
glycolipids, gangliosides

Omental lipids are made up of 97% non polar neutral triglycerides containing fatty acid types 16:0 (palmitic acid), 18:0 (stearic acid), 18:1 (oleic acid) and 18:2 (linoleic acid). Small quantities of free fatty acids, cholesterol, and di- and monoglycerides are also present.

The remaining 3%, separated by using other solvents, contains phospholipids (mainly phosphatidylcholine, sphingomyelin, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol), neutral glycolipids (mainly di-, tri-, and tetraosylceramides), complex glycolipids and gangliosides.

97% neutral triglycerides, 3% phospholipids, neutral glycolipids, complex glycolipids, gangliosides.

Pharmacological properties of omentum

Pharmacological properties of omentum

The potentially beneficial effects of applying the lipids produced in the omentum's adipocytes to areas suffering from pathologies are due to the following properties:

- *reparative effect on epithelial cell membrane;*
- *increase in microcirculation with consequent increase in blood flow to the affected area (the release of nourishing substances and removal of harmful ones is facilitated).*

The demonstration of these molecular mechanisms comes from studies undertaken in a variety of different areas, starting with the findings regarding the stimulation of new vessel production in various tissues.

At the beginning of the 20th century, long before the discoveries made in the fields of biochemistry and molecular biology, some studies were published regarding the possibility of revascularising ischaemic tissues using omentum.

In the early 1900s omentum was already being used to revascularise ischaemic tissues.

De Renzi⁷ for example, experimented on spleen tissue, while other authors studied the possibility of establishing collateral vascular circuits in the presence of heart ischemia; these collateral circuits were in part created through surgical interventions called "cardio-omentopexi"^{8,9}.

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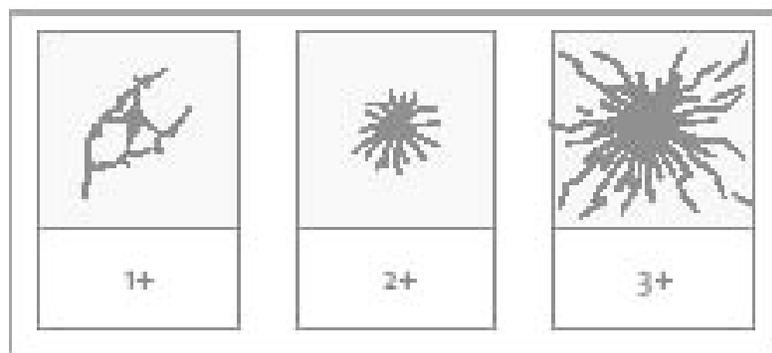
Pharmacological properties of omentum

In 1973, Goldsmith et al.³ demonstrated that vascular connections rapidly developed between nerve tissue and surgically transplanted omental tissue in the brains of animals (dogs and monkeys).

Only a few days were necessary for new vessels to develop and the phenomenon appeared even in the absence of ischaemia as the nerve tissue used in the study was characterised by normal vascularisation. Later¹⁰, preparations containing lipid fractions obtained from feline omentum through chloroform-methanol extraction showed considerable angiogenic activity when applied to the cornea of rabbits. The phenomenon could already be observed after a single administration.

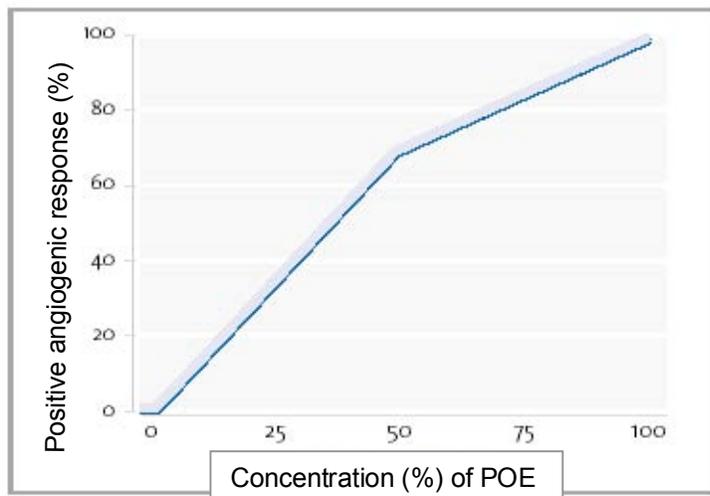
A further study¹¹ conducted on hen egg embryonate demonstrated that porcine omental extract possesses considerable angiogenic activity as measured by the Folkmann and Cotran method (Figure 3). Figure 4 illustrates the results of this study.

Figure 3 – Measurement of angiogenic activity according to the Folkmann and Cotran method.



Pharmacological properties of omentum

Figure 4 – Chorio-allantoic membrane tested with POE (Porcine Omental Extract) at various concentrations. The angiogenic response was dose-dependent.

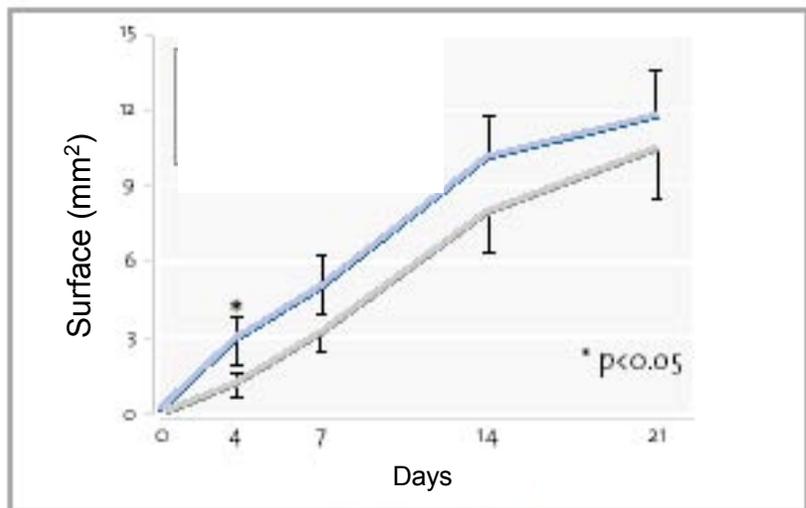
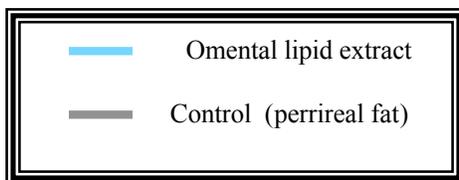


Recent confirmation was provided by a second study¹² where omental extract was injected into the cornea of rabbits: there was statistically-significantly higher neovascularisation ($p < 0.05$) in cornea where the omental extract had been injected as opposed to the control group where a lipid material from perirenal adipose tissue had been used (Figure 5).

Vascularisation observed during the study was significantly higher in the presence of omental lipids.

Pharmacological properties of omentum

Figure 5 – Area of corneal neovascularisation (mm²) in cornea treated with omental lipid extract vs. control



Omental lipid extracts stimulate *in vitro* proliferation of human endotheliocytes

The angiogenic activity of the lipid fraction contained in omentum was also observed in a study conducted on animals (cats) whereby an omental extract was injected into muscles adjacent to a surgical wound and in sites farther away. An increase in vascular perfusion was obtained as indicated by a survey of erythrocytes radiomarked with ⁹⁹Tc. The increase was unrelated to injection site¹³.

Finally, experiments were undertaken to evaluate the ability of porcine omental lipid extracts to stimulate *in vitro* proliferation of human endotheliocytes obtained from umbilical cords. The results were positive even if inferior to those obtained from external addition of bovine endothelial growth factor (ECGF)¹⁴.

Pharmacological properties of omentum

A recent study¹⁵ conducted on rats measured vascularisation induced by a lipid fraction of omentum from a different point of view: the effect on the rate of survival of skin flaps transplanted onto the backs of the rodents as measured by planimetric and histological criteria.

The rats treated with the omental extract showed considerably high rates of flap survival as opposed to the control group.

The histological examination revealed vasodilation and neovascularisation, particularly in areas between the folds and host tissue.

A summary of the results obtained during the experiments using lipids extracted from omentum is shown in Table 1.

Table 1 – Effects observed during experiments carried out using lipids extracted from omentum
angiogenic activity on rabbit cornea ¹²
increase in proliferation and migration of culture endotheliocytes and keratinocytes ^{14,16}
increase in skin flap survival in experimental animals ¹⁵
increased turnover of basal keratinocytes ¹⁷
acceleration of wound healing ¹⁸

Use of omentum in surgery

Use of autologous omentum in surgery

Omentum in experimental surgery

Starting with the experiments conducted at the beginning of the last century described earlier, and in particular those regarding the heart^{8,9}, considerable evidence has been gathered as to the omentum's ability to promote angiogenesis when transplanted onto ischaemic tissue.

Important surgical experiments were carried out on dogs by Lima et al.¹⁹ and Morgan et al.²⁰. Both authors used bronchial omentopexy techniques to reduce the risk of dehiscence or late stenosis of bronchial anastomoses during experimental lung transplants. Neovascularisation of suture areas was also accelerated.

Another study on animals²¹ examined the effect of omental lipid fraction on neovascularisation of dog spleen fragment autotransplants inside sacks made from omentum. In a group of 4 dogs the spleen fragments were immersed in omental lipid extract (referred to as "omental angiogenic factor" (OAF) by the authors), four other dogs received daily injections of OAF during the week prior to surgery, and a third group of 4 dogs received no treatment in order to serve as a control.

Angiographic and histological examinations revealed better neovascularisation and regeneration of transplanted spleen tissue in the two groups treated with omentum, confirming the existence of the angiogenic factor in the lipid fraction.

These properties were further confirmed in a study²² of angiogenesis by intrahepatic omental implantation in rat liver transplantation.

Use of omentum in surgery

Omentum in plastic and reconstructive surgery

Omentum is used for reconstruction in various situations, so much so that veterinarians have developed techniques which involve omentum transplants to promote healing of chronic wounds in animals²³.

In situations involving ischaemic limbs it is possible to use “omentopexy” to exploit omentum’s angiogenic properties.

Omentum’s reconstructive properties are the focus of numerous studies in humans in the field of plastic and reconstructive surgery.

Agarwal and his colleagues^{24,25} investigated such applications in patients suffering from Buerger’s Disease. They studied the use of omentum both by preserving its original vascularisation by means of a peduncle and splitting it in such a way that it reached the extremity of the lower limb, and by using it as a free tissue for a homograft.

The authors maintain that omentopexy is justified in multiple circulatory blocks in the limbs without supplementary distal circles when traditional reconstructive surgery is impracticable.

Omentopexy operations were carried out in patients suffering from Buerger’s Disease to promote angiogenesis; free omental tissue was used on osteoradionecrotic lesions.

In surgery of an entirely different nature, one of the therapeutic alternatives in osteoradionecrosis is omental implants. Osteoradionecrosis of the mandible is a complication which can develop following radiation therapy in the treatment of head and neck carcinoma. Free omental tissue can be literally wrapped around the damaged bone to promote revascularisation and tissue regeneration.

Use of omentum in surgery

The positive results obtained from this type of application have now placed omental transfer in the forefront of osteoradionecrosis therapy²⁶.

In thoracic reconstructive surgery, omentum has long been one of the body tissues used to close organ wounds or defects. Indications for the use of omentum in thoracic surgery include thoracic wall cancer, large sternal wounds and refractory mediastinites²⁷.

Omentum can also be used instead of pleura, thoracic wall muscle or portions of the colon in reconstructive surgery in patients undergoing esophagectomies for benign or malignant pathologies^{28,29}.

Omentoplasty used to reinforce an esophagogastrostomy following a radical esophagectomy reduced the risk of anastomosis collapse³⁰.

A technique for breast reconstruction has been developed using laparoscopically-harvested omental flaps immediately after subcutaneous mastectomies for neoplasias³¹.

Omentum grafts can be used to repair enteric fistula³² or persistent perinaeal sinuses³³ as in the case of, for example, inflammatory intestinal illnesses. The closing of perforated gastroduodenal ulcers with a patch of omentum is a standard surgical procedure³⁴.

Omentum is also used in reconstructive surgery:
thoracic wall cancer,
sternal wounds,
esophagogastrostomia,
breast neoplasia, enteric
fistula and ulcers.

Use of omentum in neurosurgery

Omentum in neurosurgery

Omentum has been used in neurosurgery for over 30 years and in numerous pathological conditions³⁵.

A treatment for Alzheimer's disease which is still in the experimental stage and practised in very few specialised centres is "omental transplantation". It consists in detaching the omentum from the structures which hold it in place in the abdomen and modifying it in such a way that it may be stretched up through the thorax and neck until it reaches the head. It is then placed directly in contact with the brain through a small hole made in the skull.

Omental transplant techniques are used in neurosurgery

The underlying theory is that the patients' cognitive function can be improved by increasing blood flow and above all by exploiting the production of omental neurotrophic factors. It is obviously a very complicated neurosurgical procedure and the risk-benefit ratio is still to be determined, so it cannot yet be systematically adopted^{36,37}.

The possibility of using omental transplants in brain surgery has recently been successfully experimented in treating serious epileptic conditions³⁸ and brain ischaemia³⁹.

Use of omentum in neurosurgery

The conclusions reached by other Authors⁴⁰ studying omental transplantation in chronic spinal lesions have paved the way for experimental use of this kind of technique in providing an alternative source of blood vessels to damaged marrow.

Finally, Heller et al.⁴¹ have recently published work in which they demonstrate the possibility of successfully managing subarachnoid-pleural fistulae by applying a transdiaphragmatic pedicled omental flap.

Topical use of heterologous purified omental lipids

Topical use of heterologous purified omental lipids

Heterologous purified omental lipids of porcine origin have proved to be of great interest for topical use in dermatology as ingredients in varying percentages in creams, emulsions and cleansers.

The activity of a lipid component with angiogenic properties can indeed be an important contribution to formulations which are already in themselves emollient and protective for the skin.

Numerous reports in scientific literature cite the topical use of purified porcine omental lipids in the management of various skin conditions.

Bertoli⁴² evaluated the effectiveness of such products in preventing decubitus ulcers during a study conducted on 210 patients confined to a bed or wheelchair as a result of various pathologies. Twenty-two of the patients presented decubitus ulcers, 45 local dystrophy, and 143 apparently unaffected skin where the medication was applied for prevention. The skin areas subject to compression were cleansed 2-3 times daily with a cleansing solution containing heterologous purified omental lipids (0.1%). After cleansing, a cream based on heterologous purified omental lipids (25%) was applied. In subjects where ulcers were present, the cream was applied to surrounding tissues.

The period of application lasted from 2-6 weeks depending on clinical evolution (average 3.5 weeks).

The properties of heterologous purified omental lipids have provide effective prevention against decubitus ulcers

Topical use of heterologous purified omental lipids

Over the course of the study, signs and symptoms such as erythema, edema, de-epithelisation, maceration and pain were rated according to the following scale:

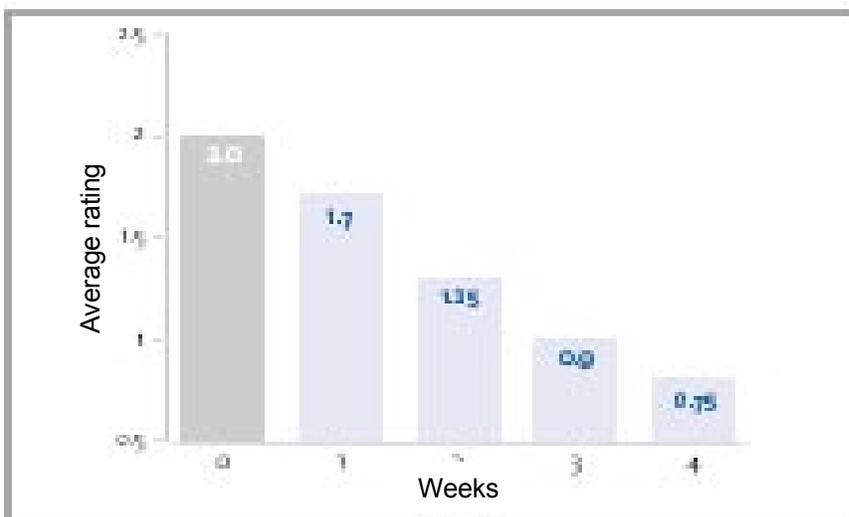
sign / symptom

absent = 0, mild = 1, moderate = 2, intense = 3, very intense = 4

After treatment, 144 patients presented unaffected skin, two patients with ulcers went into remission and 63 patients showed marked improvement in ulcers and local dystrophy. The overall improvement obtained was statistically significant ($p < 0.01$) and during treatment and afterwards there were no signs of local intolerance.

The evolution of some of the main signs / symptoms observed is shown in Figures 6 – 12.

Figure 6 – Erythema



Topical use of heterologous purified omental lipids

Figure 7 – Edema

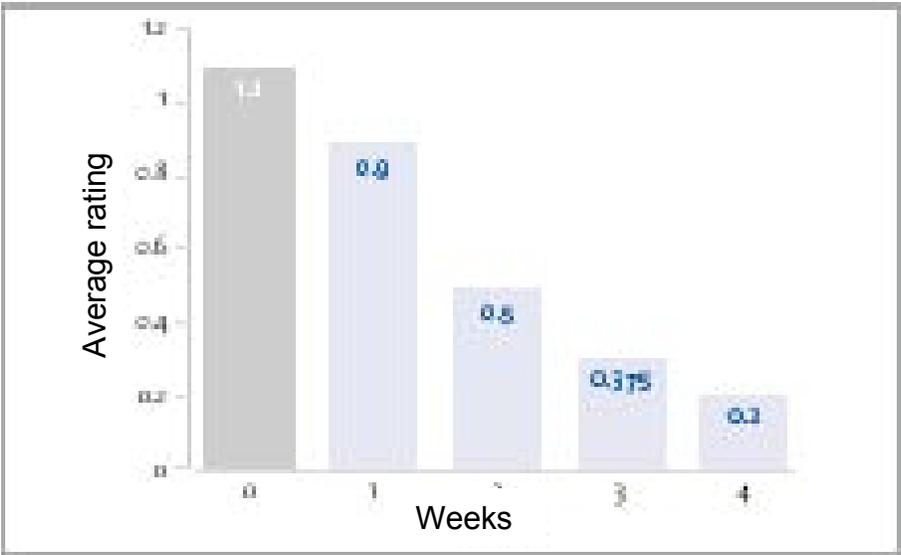
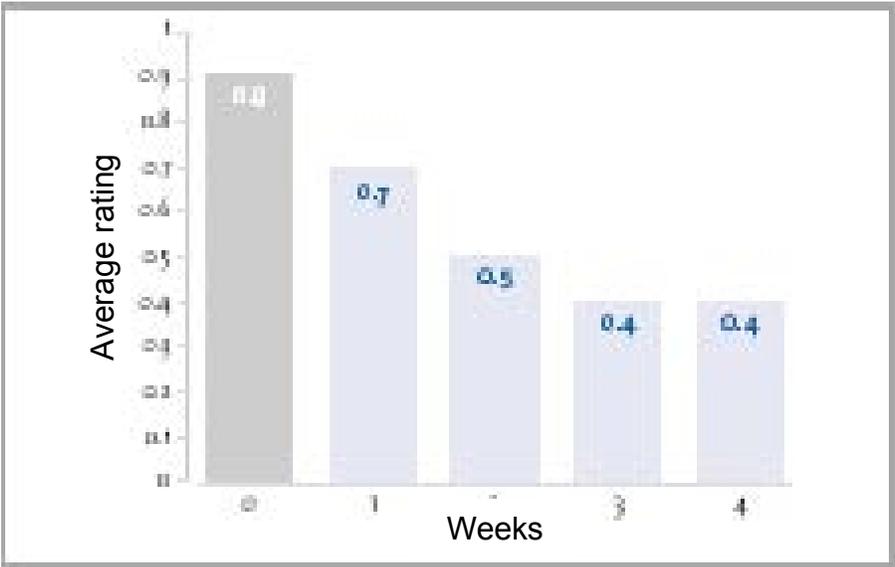


Figure 8 – De-epithelisation



Topical use of heterologous purified omental lipids

Figure 9 – Maceration

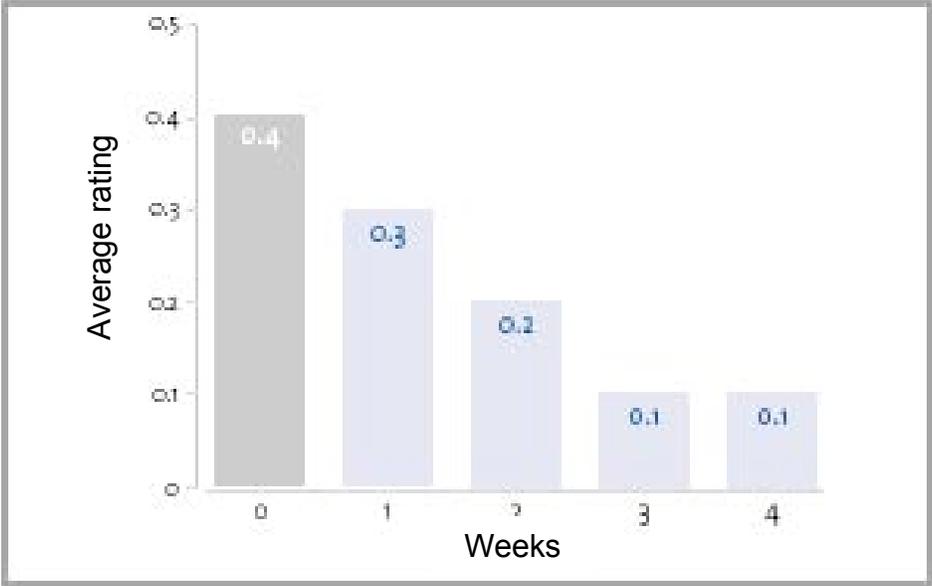
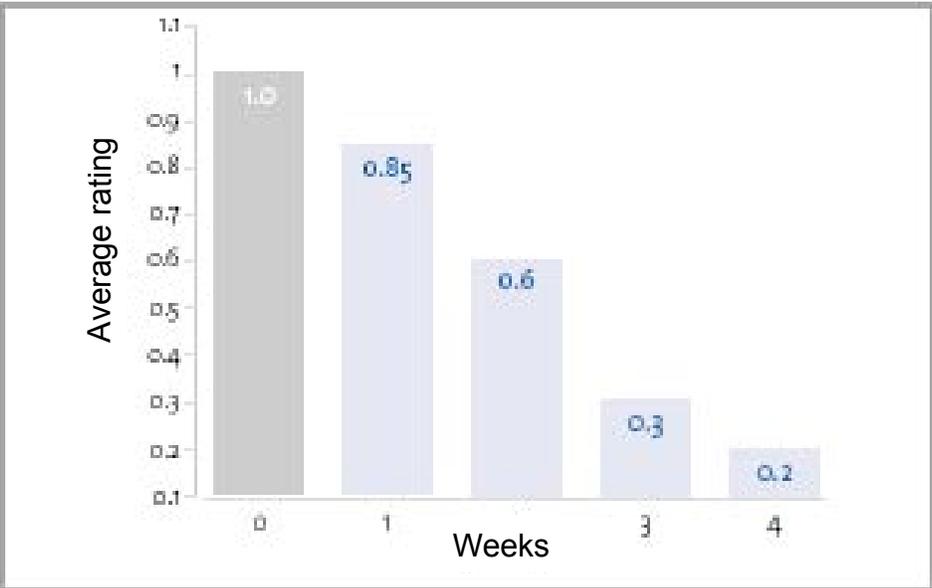


Figure 10 – Pain



Topical use of heterologous purified omental lipids

Figure 11 – Burning

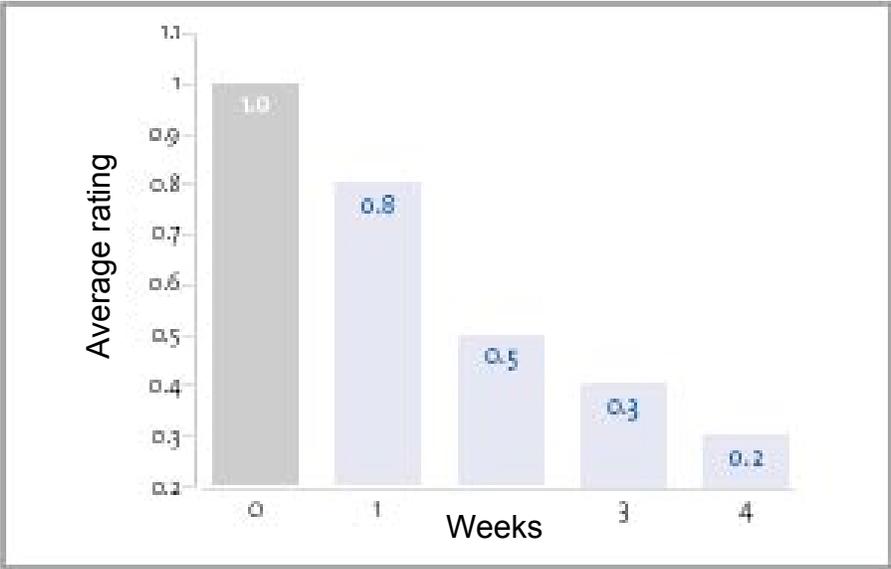
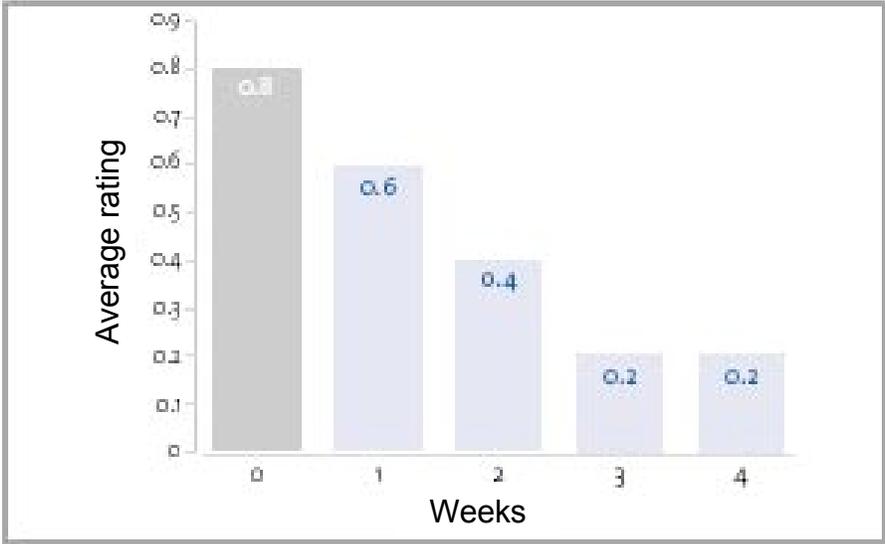


Figure 12 – Itching



Topical use of heterologous purified omental lipids

In another study⁴³ the effectiveness and tolerability of a cream and cleanser based on heterologous purified omental lipids (other components included dimethylpolysilosan, hyaluronic acid and allantoin) was tested on both bed-ridden patients at risk of developing decubitus ulcers (n=20) and on patients suffering from chronic venous insufficiency of the lower limbs (n=20).

The topical preparations were applied twice daily to areas at risk of developing ulcers and to those where varicose and/or decubitus ulcers had previously occurred. Measurements were made at the time of the first visit (T0) and then every two weeks afterwards. A final judgement was made on the treatment's effectiveness and tolerability according to the following parameters:

Studies of effectiveness and tolerability were conducted on patients at risk of developing decubitus ulcers and in patients suffering from chronic venous insufficiency.

Effectiveness:

Little	=	no preventative action
satisfactory	=	slight preventative action
good	=	considerable preventative action
excellent	=	disappearance of erythematic areas

Tolerability:

little	=	skin reaction requiring suspension of treatment
good	=	slight skin reactions not attributable to the treatment
excellent	=	no skin reaction

Topical use of heterologous purified omental lipids

Figures 13 and 14 show the judgement regarding effectiveness and tolerability.

Figure 13 – Evaluation of clinical effectiveness

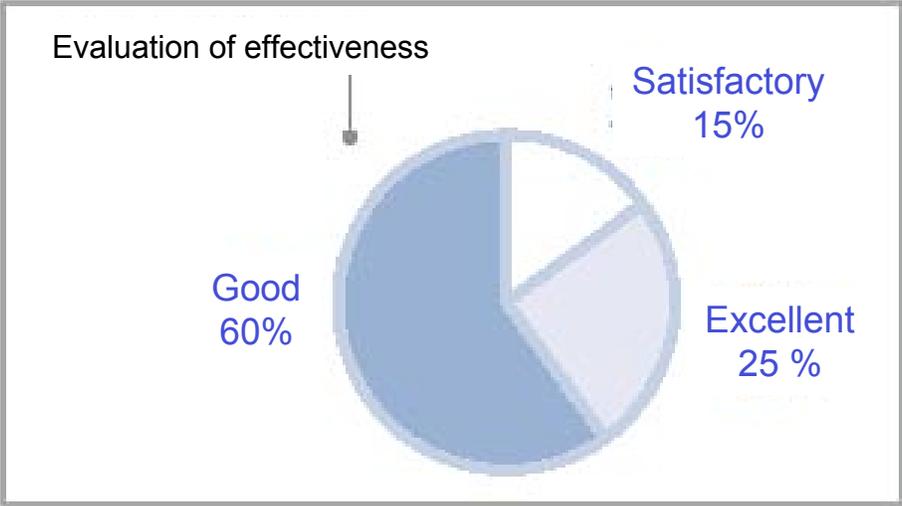
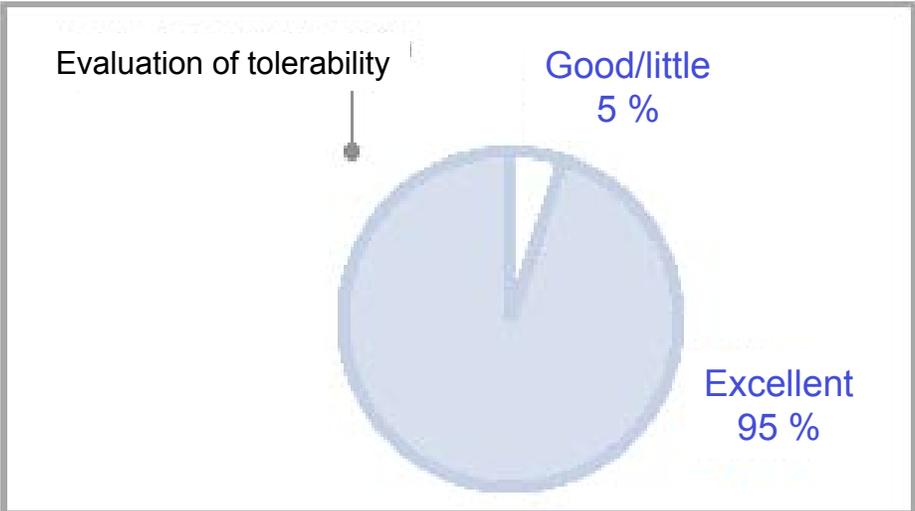


Figure 14 – Evaluation of tolerability



Topical use of heterologous purified omental lipids

The effect of heterologous purified omental lipids on wound healing was studied on healthy volunteers who agreed to submit to punch-biopsies¹⁸. Measurements were made of healing time necessary using a planimetric technique with ultrasonographic images.

Fifteen patients were enrolled in the study, each of which underwent four biopsies with 4mm diameter punches, two on the right parasacral area and two on the left parasacral area. One of the wounds made by the biopsies on each side was treated with a cream containing heterologous purified omental lipids (25%) while the other on each side was used as control.

The cream was applied once daily for 28 days even after the wounds had healed.

Measurements were made of the wounds' external and internal diameters (with a micrometer and planimeter respectively) and of their depth (with an ultrasound technique) on the first day (base) and then at 2, 3, 7, 10, 14, 21 and 28 days.

Effectiveness was judged by recording the number of days necessary to achieve complete healing and by evaluating the characteristics of the healing (no scar, pale pink scar, bright pink scar, red scar). Tolerability was also measured by monitoring adverse reactions. All parameters were examined on the basis of validated statistical techniques.

Topical use of heterologous purified omental lipids

The results showed that, especially from the seventh day onwards, the wounds treated with the cream containing heterologous purified omental lipids healed more quickly (Figure 16). The average time necessary for the healing of the treated wounds was 21.2 days as opposed to 25.1 days for the control wounds ($p=0.001$). Moreover, it was observed that healing time of the control wounds was directly related to the age of the patients: the older the patient, the slower the healing. Such a correlation was not found with the wounds treated with the omentum derivative.

Faster healing was observed in the patient group treated with products containing heterologous purified omental lipids.

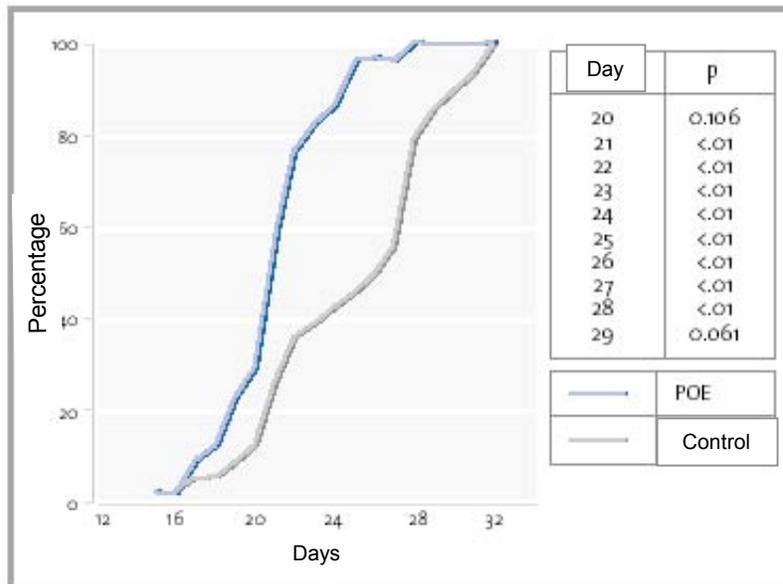
On the basis of the results, the cream containing heterologous purified omental lipids was thus shown to accelerate wound healing. In addition, it is interesting to note that the evolution of the healing was in many ways similar to experimental observations made on the Epidermal Growth Factor's wound healing activity⁴⁴.

The effectiveness of a cream containing 25% heterologous purified omental lipids in promoting the healing of difficult-to-manage diabetic foot lesions was also studied⁴⁵. In this case, the cream was applied after treatment with CO₂ or KTP lasers.

These lasers were used to promote faster healing of the ulcers and reduce symptomatology. Twenty-five patients were enrolled, all of whom were suffering from polyneuropathic ulcers and widespread skin dystrophy caused by diabetes.

Topical use of heterologous purified omental lipids

Figure 16 – Percentage of wounds healed over time



It was an open study with a follow-up period of 4 months during which skin was evaluated through measurements of Trans-Epidermal Water Loss (TEWL), comeometry, pH and sebaceous secretions (sebometry).

Topical use of heterologous purified omental lipids

In addition, eco-doppler techniques were used to study deep circulation and a laser-doppler velocimeter to study peripheral microcirculation.

The ulcers were evaluated according to their size, depth and the characteristics of their edges. Once a week photos were taken of the ulcers and measurements were made of the necrotic area.

Patients simultaneously underwent preventative treatment with systemic antibiotics.

On one of the legs, the skin areas surrounding the necrotic tissues were treated with the cream containing 25% omentum derivative; on the other, used as a control, a product containing hyaluronic acid was applied. Application of both topical products were made twice daily for thirty days.

At the end of the follow-up period, the measurements of TEWL, corneometry, sebometry and pH values all showed significant improvement on the limbs treated with omentum, while the control limbs underwent varying evolution with some slight improvements but also a few cases of worsened conditions.

Topical use of heterologous purified omental lipids

Monitoring of microcirculation with the laser-doppler velocimeter showed no changes in limbs where only hyaluronic acid had been applied, but 13 of the limbs treated with the cream containing omentum derivative experienced significant improvement with an increase of 20% with respect to baseline values. The eco-doppler velocimeter on the other hand revealed no changes in either of the groups of limbs. The improvements in the micro-perfusion observed in the treated lesions were evident 30-40 days after treatment began and reached final values by the end of the third month of therapy.

The omentum was extremely well tolerated by all patients with the exception of two who experience mild itching and for whom the applications were reduced to once a day, after which all itching disappeared.

In diabetic patients with polyneuropathic ulcers and skin dystrophy treated with omentum derivatives an increase of 20% was observed in microcirculation.

Local tolerability - heterologous purified omental lipids

Local tolerability of heterologous purified omental lipids.

As already noted, the tolerability data obtained from the clinical experiments demonstrate that heterologous purified omental lipids do not cause local phenomena of an inflammatory or immunological nature, even after prolonged application.

There were in fact few doubts that local tolerability of omental lipids on integral or lesioned skin would be good given the considerable quantity of toxicological data obtained in various animals and in various experimental conditions.

Toxicology studies⁴⁶ evaluated both acute and sub-chronic (continuous application for three months) toxicity: the results are summarised in Table 2. Furthermore, possible effects of omental lipid application on irritated skin were studied over a period of 4 months.

Finally, even though not included in the indications of dermatological preparations based on heterologous purified omental lipids, they were applied to eyes in order to evaluate their tolerability in extreme conditions.

To complete the toxicological studies, traditional testing was done with respect to mutagenesis, carcinogenesis and fertility, always with negative outcomes.

Local tolerability - heterologous purified omental lipids

Table 2 – Toxicological data for purified omental lipids.

Test	Results
Acute toxicity	DL ₅₀ >5g/kg
Sub-chronic toxicity	Negative
Local toxicity	Negative
Mutagen activity	Negative
Activity on reproduction	Negative
Ocular irritation	Not irritating

Conclusions

For many decades science and medicine have made use of the therapeutic properties of omentum. These properties had been identified on the basis of *in vitro* and *in vivo* experimental observations outlined in Table 3.

Today, however, the effects of omentum have found a consolidated scientific rationale.

Today, however, the effects of omentum have found a consolidated scientific rationale.
Possibility of creating alternative circulation by cardio-omentopexy in conditions of cardio-ischaemia
Neovascularisation only a few days after transplanting omental tissue to the brain in conditions of normal oxygenation and hypoxia
Vascularisation of corneal tissue after a single application of lipid fractions extracted from animal omentum
Vascularisation of chicken chorio-allantoic membrane tested with porcine omental extract; the angiogenic response was dose-dependent
Ability of porcine omental lipid extract to stimulate human endotheliocytes in cultures
Improved survival and neovascularisation of skin flaps transplanted onto the backs of animals using purified omental extract

Conclusions

The omentum has shown itself to be a tissue with great metabolic potential which, on the basis of the organism's needs, is able to synthesise a large quantity of growth molecules and factors, amongst which the recently-identified VEGF.

The numerous experiments conducted on animals and the surgical interventions developed for humans have demonstrated the possibility of revascularising ischaemic tissues by using omentum transplants or apposition. The therapeutic fields with the brightest prospects are plastic and reconstructive surgery and neurosurgery.

It has also been amply demonstrated that the omentum's angiogenic properties are contained in the purified lipid fraction which can be easily extracted.

Porcine omentum is an ideal source for such substances as it can provide large quantities of angiogenic and safe purified extract.

Local treatment with heterologous purified omental lipids has in fact provided significant improvement in skin microcirculation, even in the presence of severe local conditions (vascular ulcers, decubitus ulcers, diabetic foot).

Conclusions

Some of the indications which have emerged from the studies presented on the topical use of omentum are summed up in Table 4.

Moreover, the experience gained with a large number of patients has confirmed the substance's high level of safety and excellent tolerability, even when used on skin which has been damaged and is thus more likely to be subject to complications.

These beneficial properties thus place heterologous purified omental lipids amongst the most promising therapies for treating numerous dermo-epidemic pathological conditions which require skin trophism stimulation and the activation of repair mechanism for various types of lesions.

In addition to their demonstrated effectiveness in advanced stages of skin deterioration, however, are the important results obtained on skin potentially at risk: in such situations the heterologous purified omental lipids have proven to be able to prevent the development of lesions and to preserve the integrity of the skin barrier function.

Table 4 – Some indications for the topical use of heterologous purified omental lipids.

Restore and protect the skin's physiological trophic conditions

Protect the skin when it is made vulnerable (occlusion, maceration, radiotherapy, ostomies, etc.)

Treat skin in stressed conditions (dystrophy, pre-ulcer conditions, etc.)

Assist in tissue regeneration processes

CABOT P.O.L. Cream

Protect Skin At Risk

Cabot P.O.L. Cream

Based on purified omental lipids, Cabot P.O.L. Cream is recommended for skin requiring a strong emollient, protective and regenerating action. It helps quickly restore conditions necessary for optimal skin care, preventing degenerative processes and the loss of the skin barrier function. It is especially recommended for the care of the skin of people with diabetes, individuals at risk from pressure ulcers and any skin condition that has become dry, sensitive and irritated as a result of pathological conditions, environmental and external irritating agents, or specific situations such as tendency to diaper rash, prolonged immobility, radiation therapy, incontinence, ostomies, etc.

Use: apply to skin 3-4 times daily or as often as necessary. Massage Gently.

- **Diabetic Skin Care**
- **Pressure Ulcers**
- **Burns**
- **Irritation**
- **Itch**
- **Dry, Cracked, Fragile Skin**



CABOT P.O.L. Cream

Protect Skin At Risk

Ingredients

25% PURE Omental Lipids

- Stimulates microcirculation
- Improves nutrient flow to skin
- Helps skin retain moisture
- Stimulates regeneration

Dimethicone 5%

- Protects and conditions skin
- Moisture binding agent
- Beneficial in wound care

Vitamin A (retinyl palmitate)

- Antioxidant essential to repair
- Stimulates new skin cells

Vitamin E (tocopheral acetate)

- Potent antioxidant for protection
- Essential for tissue repair

Allantoin

- Healing, soothing & anti-irritating
- Stimulates healthy tissue formation
- Helps eliminate chapping, cracking
- Softens for silky & smooth skin

Hyaluronic Acid (sodium hyaluronate)

- Restores elasticity to skin
- Attracts & locks water in the dermis

Glycerin

- Highly effective humectant
- Attracts moisture
- Helps keep intercellular layer intact
- Natural barrier to retain moisture

Complete ingredient listing:

Purified Water (Aqua), Omental Lipids, Stearoxy Dimethicone, Glycerin, Stearic Acid, Polysorbate 80, Glyceryl Stearate, Propylene Glycol, Tocopheryl Acetate, Allantoin, Retinyl Palmitate, Sodium Hyaluronate, Phenoxyethanol, Methylparaben, Triethanolamine, Carbomer, Cetyl Alcohol, Propylparaben, Disodium EDTA, Fragrance



CABOT P.O.L. Cream

Protect Skin At Risk

- Enhances Circulation
- Helps Promote Healthy Skin
- Moisturizes & Rejuvenates
- Soothes Irritated Skin
- Proven Safe & Effective
- Gentle on Fragile Skin
- Non-Prescription
- Relieves Itch
- Improves Nutrient Delivery
- Softens Rough, Dry Skin



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