Collagen Materials – Collagen Processing. Technical Freedom and Scientific Challenges when Transforming Collagen into Final Materials

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Abstract

Skins are used to manufacture leather, casings and gelatine, soluble collagen for cosmetic purposes as well as medical devices like hemostyptic sponges, threads, films and matrices for cell culture.

All of these materials are manufactured from the same biological polymer - collagen. However, the skin as tissue is a natural product, a complex system far from being homogenious compared to most industrial products. Already its basic structure the collagen triple helix consists of different protein chains, there are different collagen types, the protein chains are naturally crosslinked, varying with sex, age and species, the collagen fibrils and fibre bundles vary in form, length, thickness and fiber angle over the crossection of the skin and over its area.

Nevertheless, some processing steps are common for most final materials as unhairing, liming, crosslinking, and drying. But order and intensity of these steps, the addition of some further processing stages as well as small amounts of additives are of utmost importance for the proerties of the final materials.

The lecture will give an overview on the state of the art of collagen processing and some resulting materials. The strategies to adjust final properties will be discussed with regard to known changes of the collagen structure, and open questions upon structure changes during processing will be touched.

Keywords: collagen, processing, gelatin, soluble collagen, collagen dispersion,

1. Introduction

For thousands of years, before the oil-based synthetic polymers began their triumphant advance, collagen was the dominant universal organic material used to make shoes, garments, glue, binder, filament, surgical thread and many more applications. Today, the leather market but also the food and increasingly the medical branch also ask for collagen as material. No hide is scrapped no bone thrown away, but all collagen material is used.

Leather in the view of a materials scientist references a collagen material with a broad distribution of properties from hard, almost wood–like sole leather to soft cloth-like garment leather. During leather manufacture high valuable by-products are generated which are used to manufacture further collagen materials such as casings, filaments and gelatine. The latter is used for example as adhesive, gelling agent and protective colloid, but also cosmetic additives and medical devices such as as hemostyptica, and matrices for cell culture. While the medical

market needs only small amounts of collagen raw material but with very defined quality and high requirements according to governmental regulations, the high volumes of collagen raw material are consumed by the leather and the food market. The development of new materials for the medical markets and tissue engineering however is of high scientific interest. These developments are boosted by new demands from cell biologists and by new ideas for the use and manufacturing techniques of reassembled collagen.

This contribution aims to give an overview of the structures of different collagen materials in correlation to their processing and the most important steps to adjust the final materials properties. The main focus will not be on leather but on recent research fields especially the manufacture of thermoplastic collagen and new fibrillar materials.

2. Technologies

Though leather technologies are not the topic of this lecture today, the leather industry is supplier of raw material in big amounts. The gelatine industry and the manufacturer of fibrillar materials especially the casings industry use limed flesh splits, flanks, butts and necks as raw material. Fig.1 gives an overview of the principles of different manufacturing technologies for different materials.

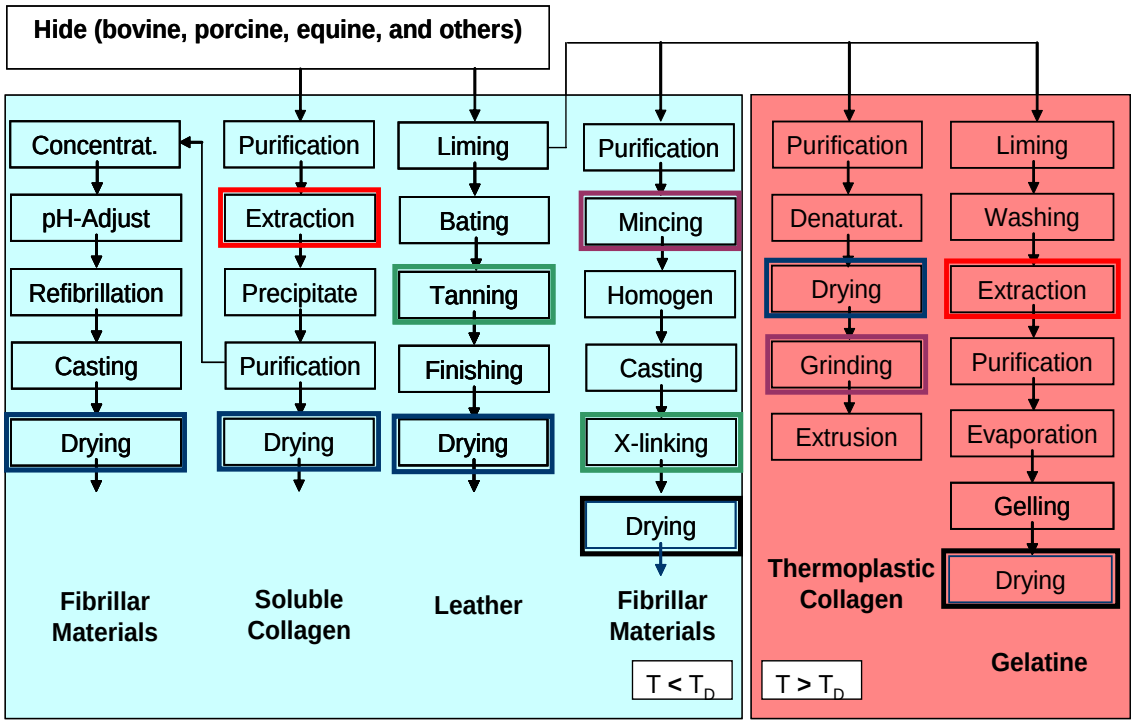

Fig.1: Different technologies to manufacture collagen materials. Processing steps to adjust final material properties are framed in bold. Not mentioned are pH and salts.

The large variety of properties of the different collagen materials is adjusted by only a few different principal steps and their succession. These are the processing temperature (a), for almost all materials the drying technology (b), pH and chemical nature and concentration of salts (c). Finally, crosslinking has the utmost influence on the processing technology and the final properties (d).

a) Temperature

Triple helical fibre forming collagen molecules denature at temperatures higher than their denaturation temperature T_D. T_D depends on many factors, e.g. the hydroxyproline content, hydration degree, pH, chemical nature of buffering salts and their concentration. But exceedingly, the collagen molecules are less stable in solution than as part of fibrils and of tissues. During denaturation one triple helical rod-like molecule in solution rearranges into three coiled molecules. In solution this transition may be followed by different techniques e.g. polarimetry, light scattering, viscometry, chromatography and also differential scanning calorimetry (DSC). However, the latter is one of the rare techniques by which the transition may also be followed for non-soluble samples e.g. skin, tendon and also leather.

Other than previously published (Meyer et al. 2005), during denaturation the collagen specific D-periodicity does not necessarily get lost. It seems that this D-stagger may show only slight reduction while the the triple helices already show advanced partial denaturation (measured by AFM and DSC) (Schröpfer and Meyer, 2011).

Though the primary structure of collagen has been discovered decades ago and the triple helical structure has been resolved, the mechanism of its stabilization is still a subject of discussion. On one hand hydrogen bonds and water bridges in combination with external water molecules are discussed, on the other hand inductive effects and electrostatic interactions are seen as main stabilizing influences (e.g. Brodsky and Ramshaw 1997; Jenkins and Raines, 2002; Engel, 2004).
The technologies of treating collagen materials may be structured into two main groups, denaturing ($T>T_D$) or non-denaturing ($T<T_D$). The raw material is denatured to manufacture gelatine and thermoplastic collagen, the technologies working with native collagen comprise leather, fibrous materials and the processing of soluble collagen.

b) Drying

Drying of collagen materials aims primarily to stabilize them against microbiological attack. However, the drying technology has big impact on the final properties. Fibrillar materials may be convection dried as well as freeze dried. During convection drying the water filled pores of the collagen structure collapse because of capillary forces. The collagen chains stick together, which leads to stiff and sometimes brittle materials. Collapsing of the pores may be prevented by solvent drying or by freeze drying. The resulting sponges become soft but stability is limited. Because all collagen preparations contain high amounts of water the drying step is energy consuming and therefore often the most expensive processing step. Gelatine is usually dried by spray drying, convection drying or in some cases also by freeze drying. Fibrillar materials are convection dried in long drying tunnels or are freeze dried.

c) pH and salt

pH and chemistry of buffer salts strongly influence the thermal stability of fully hydrated collagen (Hayashi and Nagai, 1973; Komsa-Penkova et al, 1996; Schröpfer 2012 see Fig. 2). This is important when adjusting the conditions during wet grinding and convection drying at elevated temperatures.

Alkaline and acidic pH charge the molecules, the protein chains repel each other and the materials begin to swell. The increase of stability in neutral range is presumably caused by entropic stabilisation of neighboring triple helices of the fibrils.

Salts may behave as chaotropes or kosmotropes. The former as well as organic lyotropica destabilize water shells and hydrogen bonds (e.g. Urea, $CaCl_2$), the latter stabilize the structure (phosphate, sodium sulfate). This behaviour is concentration dependent and discussed in detail by Kunz (2010). Background reference is the Hofmeister series. Therefore, as known by tanners for many years, the chemical nature of the added salt and its concentration strongly influences the process stability. It may however also be used as a regulating variable during processing.

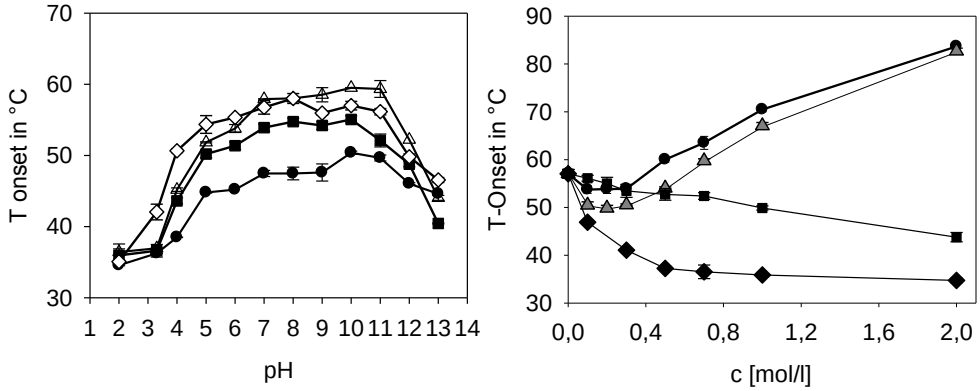

Fig 2: T_{onset} (~T_D) of fully hydrated samples (left) vary with the pH; ●..acid soluble collagen (ASC); Δ...rat tail tendon (RTT); ◊..bovine hide; ■..porcine hide; sodium citrate buffer. T_{onset} of skin (right) is dependent on the used buffer salts (pH 7) and their concentration (●..Phosphate; ▲..Na_2SO_4; ■..Urea; ◊..$CaCl_2$) (Schröpfer 2012).

d) Crosslinking

The largest part of collagen in collagen raw materials is naturally crosslinked (Bailey et al. 1998). This is the reason why collagen cannot be solubilized easily. Collagen materials are mostly further crosslinked synthetically by bifunctional synthetic chemical crosslinkers, enzymatically, by metal ions, and other mechanisms. This broad field is intensively studied by tanning chemists and biochemists and recently summarized by Covington (2009). Crosslinking by physical methods may be achieved by UV, temperature treatment in dry state, radiation and electronbeam.

Briefly, crosslinking decreases solubility, susceptibility to enzymes and microbiological attack. It increases the hydrothermal stability and the mechanical properties, especially in the wet state.

2. Materials

Extraction or full substance?

Gelatine as well as soluble collagen are extracted from raw material in batches. The aim of the procedures is to solubilize all raw material which is achieved by partial hydrolysis of the

collagen. The resulting solutions are much easier to characterize than the insoluble materials which has therefore been widely done. However, these procedures are long lasting and the yield of the high qualtity extracts (usually the first extracts) is low.

In contrast, when treating full substance hair-free collagen raw materials (tendons and pelts) they may also be coarsely ground and minced to manufacture fibrillar materials. The technological requirements concerning purification and homogenisation are much higher.

While the manufacture of soluble collagen is a special case, which will be discussed later, all other technologies are basing on limed material supplied by tanneries. The hides are unhaired and the collagen structure has already been opened up. Asparagine and glutamine are partly deamidated, the isoelectric point has decreased, non collagen components such as proteins and glucosaminoglycans have been extracted. The limed pelts are usually split and trimmed. These by-products are used for further processes.

3.1 Solube collagen

Soluble collagen in different states is extracted from fresh raw hides (mostly calf) without preceding liming in the cold by organic acids (acid soluble collagen, ASC), supported by peptidolytic treatment (atelocollagen, ATC) succeeded by exposure to strong alkaline (desamidocollagen, DAC). The aim is to solubilize all collagen from the raw material. This lasts several weeks up to months and requires sufficient preservation of the batches. Acid soluble collagen is the least attacked collagen, only acid susceptible native crosslinks are cleaved. Pepsin digests the telopeptides. Non-acid cleavable native crosslinks, which are located in the telopeptides, will be destroyed (Bailey and Light, 1989). The remnant which is exposed to alkaline solublizes during this last step and asparagine and glutamine are deamidated. The solutions may be purified easily by established techniques such as filtration, precipitation and ion exchange.

3.2 Gelatine

Gelatine is manufactured from non-limed porcine skins by an acidic hydrolysis (type A gelatine) and from demineralised bones (ossein), limed bovine splits and trimmings (type B gelatine). The technologies are described elsewhere in detail (Ward and Courts, 1977; Schrieber and Gareis, 2007). Briefly, to manufacture type B gelatine limed raw materials from tanneries are treated with alkaline (gelatine liming) for further weeks, the alkaline raw material is delimed, washed, extracted with hot water at different temperatures (sequence of extracts), the extracts are purified by sieving and desalted by ion exchange, concentrated by evaporation and dried.

The gelatine liming leads to the topochemical cleavage of natural crosslinks which increases the yield especially of the first extracts (Babel, 1996). These first extracts show the best gelling behaviour and the highest viscosities.

The gelatine technologies have been a research field for a long time especially when it was still used in the photographic industry. The international IAG conferences had been the most important scientific conferences until 1996. Topics have been physical properties (gelling behaviour, viscosity), analytical topics (chromatography, viscosimetry, impurities) as well as technological aspects (e.g. Brass and Pouradier, 1993).

This changed with the broad implementation of digital photography. Today, the main use of gelatin is in the food sector to bind water, as gelling agent, as thickener to achieve the right mouth feeling e.g. in meat industry and in wine gums. Further properties comprise stabilization and forming of emulsions, foams and films and the use as protective colloid. Smaller amounts are already used for decades as encapsulation material for pharmaceuticals (Schrieber and Gareis, 2007). Most of the basic research has been shut down inbetween, however. The supply with new raw material sources especially fish are recent developmental tasks.

3.3 Fibrillar materials by tissue grinding

The main final product group prepared from native collagen fibers are casings. To manufacture the needed fibrillar raw materials limed splits, necks and butts are delimed, coarsely ground and further homogenised. The homogenisation is achieved differently depending on the technology (Hood, 1987). The yield of these processes is very high, because full substance raw material is used.

During the so called dry process the coarsely ground fibers at pH 3 are pressed through a cascade of perforated discs. The resulting dispersion shows high viscosity, a dry matter content of 7..12% and contains fiber bundles up to centimeters in length. Plasticizers, flavours and further ingredients are added in big mixers to these dough-like dispersions, which are then extruded with specially designed cold dies into tubes. The tubes are neutralized, the collagen is crosslinked (by smoke or glutaraldehyde), dried, rolled up and packed (Maser, 1996).

In comparison during wet technology the fibers are homogenized at pH 4-5 using colloid mills. During homogenization further ingredients are added. This means that mincing and mixing is performed in one step. Then it is necessary to acidify the mass to improve swelling and to adjust viscosity. The dry matter of the mass content is 4.5...6 %. The mass is extruded as a tube in a chamber with gaseous ammonia and flooded with concentrated salt solution to precipitate the collagen. It is washed by bathing with plastiziser (glycerol, sorbitol, dextrose) and crosslinker and finally dried in a convection tunnel (Hood, 1987).

A third technology to manufacture casings which becomes more and more important is coextrusion. A collagen dispersion prepared from disintegrated collagen This collagen is partly denaturated and it is extruded simultaneously with the meat dough. To achieve sufficient stability the sausages are then soaked in brine to dehydrate the casing and the latter is crosslinked with smoke condensate. The technology is very cost effective, needs special machinery however and the stability of these casings is less than of those manufactured by dry and wet technology (Niemeijer, 2003).

3.4 Sponges

Minced collagen similar to that used for casing manufacture is used as starting material to manufacture sponges by freeze drying collagen dispersions. The sponges may be physically crosslinked by dehydrothermal treatment subsequent to the freeze drying procedure (Weadock 1996; DE4028622C2). The pore sizes of the sponges are determined by the freezing procedure. Fast freezing leads to small ice crystals with small pores remaining after sublimation of the ice, long lasting freezing increases these pores.

Such sponges are used in the cosmetics industry to soothe irritated skin as well as to achieve hemostasis in surgery and dentistry. In contrast to gelatin sponges, native collagen is able to trigger hemostasis chemically by activation of the coagulation cascade (Jesty et al., 2009; Kehrel, 1995).

Recently, to circumvent the expensive freeze drying technology of manufacturing medical sponges a technique was developed to whip such collagen dispersions physically (Meyer and Trommer, 2013). Native collagen dispersion has no foam stabilizing property. Therefore, warm gelatine solution was added to these dispersions as foaming additive. If the temperature of the mixture of collagen dispersion and gelatine is lower than the denaturation temperature of the fibers this mixture may be whipped physically e.g. by mixing devices or by air injection. The gelatin sets and the collagen fibers remain native. The sponge combines the hemostyptic properties of native collagen with the foaming properties of gelatine.

3.5 Fibrillar materials by fibril reconstruction

Almost one hundred years ago native acidic soluble collagen was especially used in laboratory scale to study the basic structure of collagen (Bowes, 1955). Soluble collagen has been used for decades as an additive in cosmetics. Recently this native soluble collagen was used as precursor to generate fibrils again to manufacture new materials.

The reassembly of collagen fibrils in vitro has been studied in the early 1960s by Wood (1960) and more intensively the fibril morphologies were investigated by Holmes et al. (1986). To achieve fibril forming an acidic collagen solution in the cold (e.g. 4°C) has to be warmed up and neutralized. Therefore two routes may be used for this process, the "neutral start" route in which the collagen solution is neutralized in the cold and then warmed up and the "warm start" route, when the tempered collagen solution (e.g. 30°C) is mixed with buffering solution at the same temperature. Fibril assembly may be folowed by turbidity measurements in a thermostated spectrophotometer at 313 nm. Kadler et al. (1996) resume that this process is entropy driven similar to other protein reassemblies.

Bradt et al. (1999) first tried to use this reassembly technique in vitro to biomimic mineralization of collagen similar to bone. They added calcium ions to the acidic starting solution of collagen and phosphate to the neutralizing buffer. During the above mentioned reassembly procedure simultaneously with collagen fibril forming amorphous calciumphosphate was precipitated which further recrystalized into hydroxyapatite. The procedure was varied by freezing the composites and subsequent freeze-drying of the bodies and stabilisation by cross-linking (Gelinsky et al, 2008). This lead to porous scaffold similar to bone which could be seeded with cells.

Reconstituted collagen fibrils were furthermore used to manufacture silicified collagen hybrid materials for bone replacement. The reconstituted fibril gel was dialized against water, lyophylized and these fibrils used as starting material for silicification. The collagen was resuspended in buffer, TEOS (Tetraethoxysilane) was prehydrolysed and intensively mixed with the collagen suspension to achieve a final ratio of 30% collagen and 70% SiO_2. Then the mixture was cast in cylindric vials and dried. In parallel to this drying procedure the prehydrolysed TEOS condensates into amorphous silica and the volume decreased by 90% because of the loss of water. This drying has to be performed stressless to get monolithic bodies. These bodies are biocompatible, very slowly biodegradable, they show mechanical

behavior like bone (elasticity, strength) and can be described as fiber reinforced ceramic composite. The technique allowed manufacturing small cylindric bodies of 1 cm³ (Heinemann et al. 2007).

Finally, Jiang et al. (2004) were able to assemble collagen microfibrils in parallel and they precipitated this collagen on mica surfaces. They showed, that adsorption on the surface depended on pH and the ion composition in the fibril forming buffer. This technique was only established in lab scale to achieve samples for AFM investigations. The challenge will be to generate fibers and fibre bundles and basing on this fleeces, films or non wovens with oriented structures. This would allow specially designed collagen materials with defined physical structures and predetermined anisotropies.

3.6 Fusion of fibrillar technologies

The disadvantage of reconstituted fibrils is the necessary use of collagen solution as starting material. This collagen in contrast to the ground fibrillar materials, is very expensive and the manufacturing technologies are complex when mimicking biomineralisation. Therefore, we investigated silicification with minced collagen dispersion as described above (Heinemann et al. 2007b; Schröpfer et al., 2011). Small as well as bigger monolithic devices up to 10 x 10 cm could be manufactured. The reproducibility decreased with increasing their size, however. It seemed that the homogeneity of the dispersions prepared from grown tissue is much less that that of reassembled collagen fibers.

3.7 Textiles

Filaments of collagen have been prepared by precipitation from collagen solution as well as from dispersions. Collagen filaments were developed recently by Zeugolis et al. (2008; 2009) but the filaments were not stable enough to manufacture textiles (for a summary see Meyer et al. 2010). Therefore, we developped a technique to prepare filaments from collagen foils prepared from minced solutions by cutting them into small ribbons and further twisting. These filaments could further be processed by textile techniques such as weaving and knitting. The woven structures showed similar mechanical properties under physiological conditions as polypropylene non-wovens to be used for surgical purposes (Meyer et al, 2012).

3.8 Thermoplastic collagen

Limed bovine pelt, which is dried and ground in native state leads to fibrous cotton wool-like material. Partial denaturation of this pelt with subsequent fine grinding becomes collagen powder, which can be processed by established thermoplastic technologies of synthetic polymers, such as extrusion, injection moulding or film blowing. Therefore, this partially denatured material was called Thermoplastic Collagen (TC) (Meyer and Kotlarski 2005; WO 2007104322).

The technique is not limited to bovine material, but has also been successfully performed with porcine TC and can probably be expanded to other species. Viscosity measurements of the melt under extrusion conditions showed that TC can be considered as a thermohydroplastic material. The properties of the protein melt and its plasticity mainly depend on the raw material and the type of the denaturation process. Denaturation by hot water, by heating in an oven, by microwave and by direct extrusion have been investigated in comparison (Klüver and Meyer, 2012).

It appears that denaturation by extrusion degrades the material to a great extent such that the extrudate shows decreased mechanical stability and cannot be blown to large-scale films. Denaturation in hot excess water is an energy consuming batch process, which is coupled with loss of collagen by dissolution and cannot be completely controlled, yielding TC of varying quality. The optimal degradation technique appears to be microwave treatment, which can be easily performed as a continuous process. Its efficiency is comparable with the hot excess water process.

Plastification of thermoplastic collagen can be achieved only by addition of a considerable amount of water as plasticizer. Other useful additives are glycerol as permanent plasticizer and stearic acid as lubricant. Collagen melts can be processed into various forms, like strands, threads, bands or films. However, the low mechanical strength and high moisture sensitivity of pure TC products demand additional treatment, like crosslinking or blending with synthetic polymers, in order to improve these properties.

Potential applications of TC based products have been tested in different technical sectors. Mulchfoils were manufactured by film blowing in combination with Ecoflex®, a synthetic biodegradable copolyester. The biodegradability of the blends was adjusted by the content of Ecoflex®. The more Ecoflex® was used the higher was the stability. The degradability in the field ranged from several days to seveal weeks.

By injection moulding flavoured dog chews were produced. With this technique also complex articles could be manufactured. Further applications might be food packaging and medical devices. We were concerned about the structure of such material after extrusion. It is mostly denatured collagen but is not soluble as a gelatin presumably because of remaining natural crosslinks or new ones which are formed during extrusion. From rheological and calorimetric measurements it was concluded, that this materials behaves like an interpenetrating network, consisting of a physical and a chemical gel. The physical gel behaves like a high molecular gelatin (Meyer and Kotlarski, 2005).

The combined extrusion with hydroxyl apatite (70%) with TC (30%) led to strands, which behaved in a tough and rigid way, when dry. The material was able to be machined by drilling and lathing into screws and cylinders. The idea to use this as bone implant failed however, because after soaking in physiological buffer the devices became gum-like.

3.9 Medical devices

Medical devices from collagenous tissues are manufactured from a broad variety of collagen raw materials, not only skins. The submucosa of gut is used as well as pericard, fasciae of diverse muscles, tendon, ligaments, heart valves and skin. These raw materials usually come from mammals e.g. bovine but also others (Olde-Damink, 2003).

When manufacturing medical devices it is important to think about sourcing of the raw material, the purification procedures, the sterilisation and the final certification. If bovine raw material is used it has to be sourced from BSE free countries. To manufacture those biomaterials all strategies and techniques are used which have been mentioned above. Some examples are: cellfree tissue eg. skin (Xenoderm®), crosslinked pelt (Permacol®), ground fibrils cast into compact films (Gentafoil®) and sponges (Matristypt®). Furthermore the tissue or fibers are thermally denatured and gelatine sponges are manufactured by freeze

drying and crosslinking. Also collagen from solutions is used as it is or the collagen is reassembled to achieve fibrils.

In the medical field the major challenge beside the technical requirements is usually to certify the final product. In Europe the tissue itself has to be sourced and qualified according to EN 12442 (Animal tissues and their derivatives utilized in the manufacture of medical devices). The collagen materials have to be manufactured according to DIN EN ISO 13485 which regulates the documentation of the processing procedures. Furthermore, purity, biodegradability and biocompatibility have to be tested comprehensively (e.g. according to ISO 10993 (Biologische Beurteilung von Medizinprodukten); ASTM F2212-11 (Standard Guide for Characterization of Type I Collagen as Starting Material for Surgical Implants and Substrates for Tissue Engineered Medical Products (TEMPs)). Finally, the admission board has to evaluate the complete procedures of development and manufacturing to award a certificate for medical devices.

4 Comparison of the materials

The presented materials can be ordered according to their thermal, mechanichal and chemical disintegration (Fig.3). Leather is the least decomposed material. The fibre structure is saved and even further stabilized by crosslinking. The most cleaved materials are gelatine hydolysates. They neither show fibre structures nor triple helix structure (as soluble collagen). Hydrolysates have been treated intensively by thermal, mechanical and chemical processes.

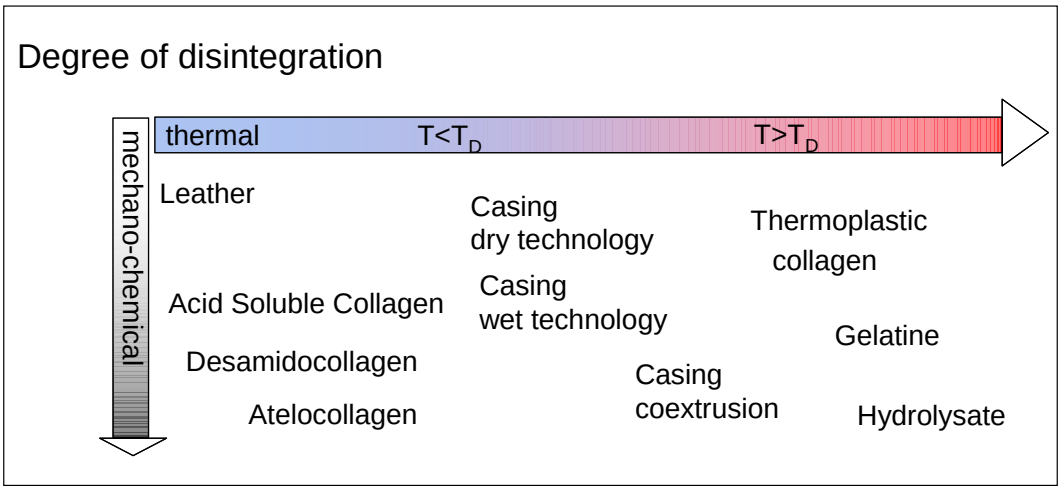

Fig.3: The collagen materials regarding their disintegration.

A comparison of the resulting materials in dry state under the SEM is summarized in Fig.4. There is almost no difference visible between the the casing, TC-filament, and the gelatine even though the former shows native fibrils and is insoluble. The latter had been denatured. They are partly and fully soluble in hot water, respectively.

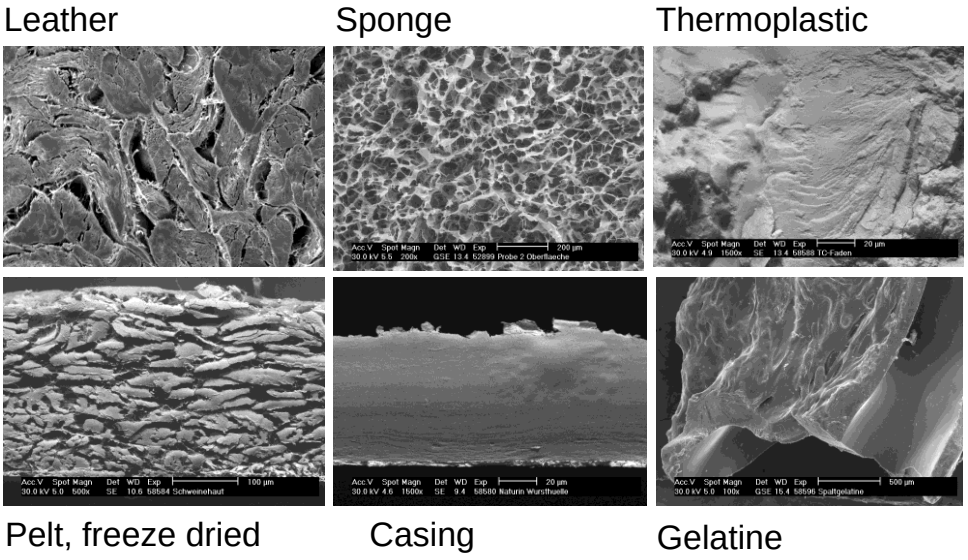

Fig.4: Scanning electron microscopic images from different collagen materials in dry state.

The difference between the lyophilized skin and the sponge is that collagen for the sponge has been minced before drying. Therefore, the original fibrous structure has been exchanged for a structure, which is determined by the freezing process. The difference between sponge and casing is only the drying procedure. The collagen fibre structure collapses during convection drying (casing), while it is saved during freeze drying. Finally the structure of the leather differs from that of the dried pelt in that the leather pores are filled with fats. The fat prevents the fibres from collapsing. Surely during tannage the fibres are further stabilized.

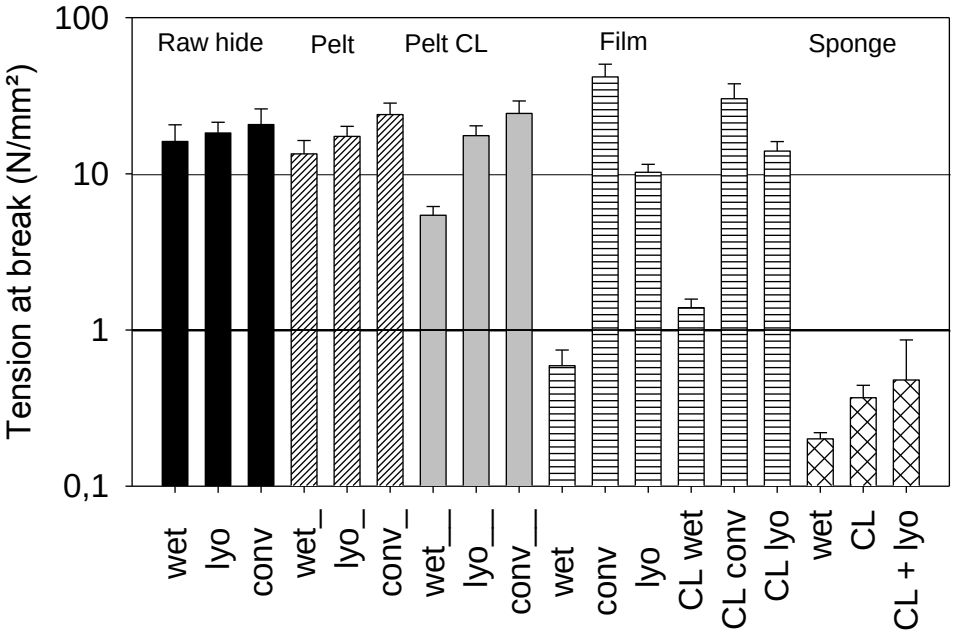

Fig. 5: Comparison of the tension at break of different collagen materials. CL.. crosslinked by glutaraldehyde 0.1 %; conv..convection dried; lyo..freeze dried

If these materials are compared regarding their tension at break the influence of different processing steps may be impressively demonstrated (Fig.5). The wet stability is usually lower than the stability in dry state. Raw hide shows the highest stability. Liming and further processing does not affect stability in dry state, but in wet state these processes decrease mechanical stability. Films, which were manufactured from minced collagen show much lower tension at break than the raw materials (pelt) before mincing. The mincing process therefore destructs the fibers as stabilising components. Interestingly a dry film shows higher tension at break than the original hide. The fibers stick together which gives additional stability and the films are thin, around 40 µm. The tension at break is evaluated in regard to the sample thickness.

However, if this sticking of the fibers is (partly) prevented by freeze drying (lyophilizsation) the breaking tension becomes lower again. Wet sponges which reflect highly porous structures from minced collagen show the lowest tensions at break. The stability can be slightly improved by crosslinking.

All data of Fig. 5 reflect an evaluation with regard to the thickness of the samples. Depending on the final use of the materials the absolute forces may be of interest. As an example, surgeons require materials which can be draped, sewed, which are biocompatible, biodegradable but the thickness can be widely neglected. We therefore compared the forces at break from different originial tissues and collagen materials (as an example see Fig. 6).

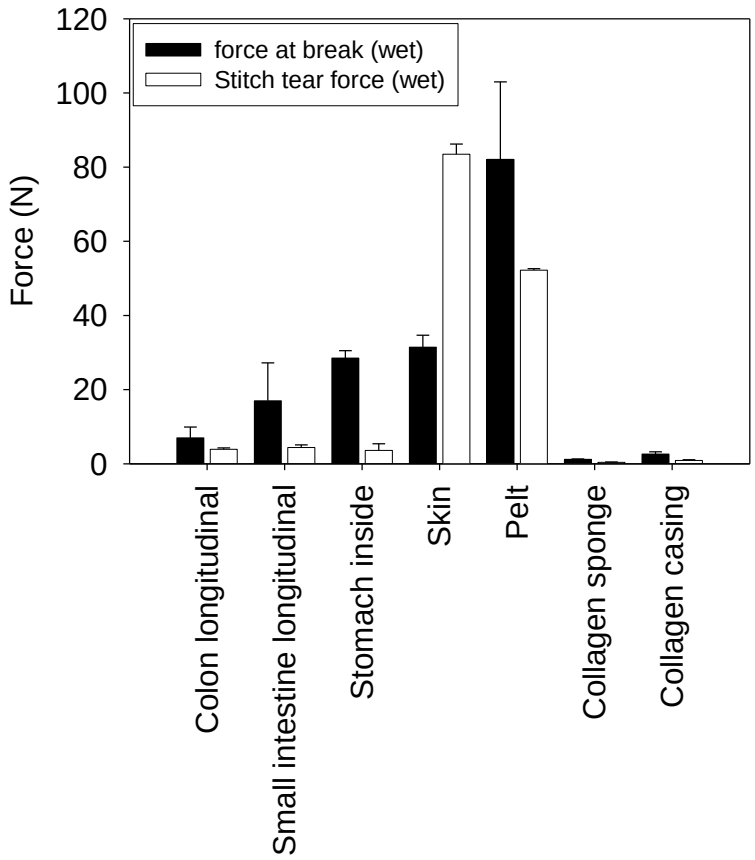

Fig 6: Tear forces at break and stitch tear forces of different collagen materials for surgical purposes in comparison with living tissue, measured after swelling in 0.9% $NaCl_{aq}$.

It is important that all of these values are measured in wet state similar to the conditions of use. The skin shows impressively high strength, by liming this strength is reduced. The mechanical properties are by far higher than that of intestine and also the inside layer of stomach. The collagen materials which are manufactured from fibrillar material show much lower strengths than the intestines. Interestingly, the stitch tear strength which is also a parameter which interests surgeons, varies very much. Especially collagen

degradation even in liming state has a big influence. But already the original tissue (intestine) has a low sewability.

5 Outlook

This contribution aimed to present some less known technologies to manufacture collagen materials and the comparison of some properties. It was shown, that collagen allows a very broad use but with some limitations. First, the structure of the final materials is determined by that of the raw material used. Up to now with some exceptions only preceding disintegration is possible. A second important property of collagen is its hydrophilicity – it is a limitation and an opportunity. It is a limitation when collagen materials have to be compared with synthetic polymers for technical purposes. Then, the (thermo)stability is not sufficient for many uses. It is an opportunity regarding biocompatibility and biodegradability and when binding of water is the intended use.

What are the scientific challenges?

To achieve a much better understanding of the materials properties it seems necessary, to learn more about fibre structure, weaving angle and other stabilising factors of the raw material and regarding skin in the different layers. This should be directly correlated to the mechanical properties and hydrothermal stabilities of the final materials in dry and in wet state.

Though mentioned in the beginning, that the skin is non-homogenous, the physical stability is much higher than that of all other materials, which have been manufactured from disintegrated collagen. It remains an open question whether this may be overcome by oriented reassembly of the collagen by technical procedures.

The mineralisation of collagen is a very specific field to manufacture medical devices, which has only recently begun to be established. The hydrothermal stability of bone and that of mineralised devices is much higher than that of skin, however. The knowledge about the structuring ability of collagen molecules to form inorganic matrices may be used in future to learn more about the inorganic tannages – and maybe especially that of chromium.

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