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3,055,790 HYDROXYLAMINE TREATMENT OF COLLAGEN FIBERS

Roger de la Burde, Chicago, and Arthur Veis, Skokie, Ill., assignors, by mesne assignments, to Armour & Company, Chicago, Ill., a corporation of Delaware

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This invention relates to the disaggregation and delamination of collagenous structures by hydroxylamine, and to novel chemically modified and highly reactive fibers of collagen.

Collagen is the primary intercellular protein constituent of the white connective tissue in animal tissues. Skin, tendons, reticular tissue, bones and various other animal structures contain interwoven networks of collagen fibers which are highly organized in the native structures. Hydrolysis and other drastic chemical treatments normally melt or destroy the organized structure without releasing fibers in an intact form. Each fiber is ordinarily locked within the woven structure and tenaciously adheres to contiguous fibers.

Chemical modification, or tanning, of collagen to produce leather is traditionally performed on intact animal skins. During fabrication of leather goods, scrap leather resulting from the fabrication, plus defective skin areas which must be discarded, represents economic loss to the fabricator. It is therefore highly desirable to have available homogeneous collagenous raw material which may be reassembled into desirable structures without formation of waste material and which utilizes leather scrap. Because cost of fabrication is further increased by variations in thickness and shape of leather pieces, it is desirable to have available a method for reassembling collagen into skin-like structures of uniform thickness and shape.

Previously, attempts have been made to prepare collagen structures, such as sheets, from reconstituted collagen. Heretofore the most promising method of preparing reconstituted collagen involves dissolving the procollagen fractions of collagen and re-precipitating these dissolved fractions in the present of undissolved fibers to give the resulting mass strength and cohesiveness. Difficulties have been encountered in attempting to obtain strong and intact undissolved fibers. Previously, native collagen has been mechanically beaten to break fibers from the organized collagen structure. This mechanical beating results in cutting of the fibers, the shorter fibers in turn result in formation of lower strength reaggregated material.

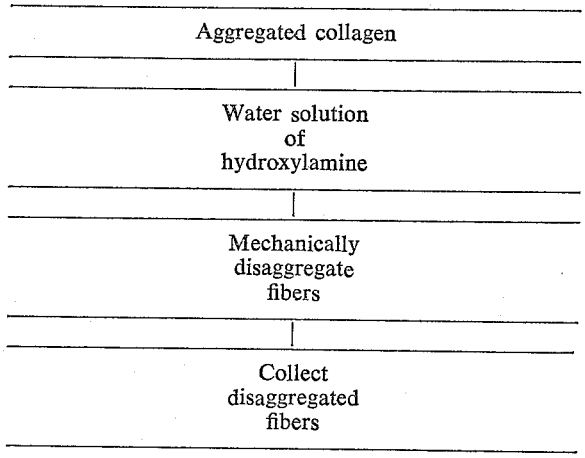
We have invented a method for delaminating, or slipping, and chemically modifying fibers in collagen aggregates in a manner whereby the individual fibers may be slipped from the network of the collagen structure without disintegration or degradation of the fibers to yield fibers having the basic physical properties of collagen, but the fibers being chemically modified to render them highly reactive.

An important object of this invention is to provide chemically modified fibers of collagen which are susceptible to reaggregation into desired skin-like structures. A second object is to provide a process for disaggregating aggregated collagen structures to thus prepare a homogeneous supply of collagenous fiber stock suitable for reaggregation. A further object is to provide collagen structures having the basic physical properties of native collagen but which are chemically modified so as to be highly susceptible to inner reaction with various chemical reagents.

Our method generally involves the reacting and conditioning of aggregated collagen with hydroxylamine solution, mechanically manipulating the conditioned collagen,

and collecting disaggregated and chemically modified fibers.

A simplified flow diagram of the process is as follows:



Suitable starting materials which we may use include collagen from various sources that has been exposed to various treatments. For example, traditional sources of leather stock such as calfskin, cattle hides, pig skins, etc., which have or have not been limed and/or enzymatically conditioned and the like may be used. Moreover we may use ordinarily less useful sources of collagen, such as tendons, bones, reticular tissue and detanned leather scrap as sources of our fibers.

Hydroxylamine, NH_2OH, interacts with the individual fibers of a collagen aggregate to so chemically modify them so that they are no longer capable of adhering to one another as they normally do, as a consequence of which the fibers slip from the structure without being markedly physically affected during the process.

We prefer to use a water solution of hydroxylamine having a concentration of about 20 to 80 percent hydroxylamine by weight in water. Collagen may be immersed in the solution of selected strength for varying lengths of time and at temperatures up to about 60° C. to give the desired conditioning effect. Hydroxylamine is somewhat unstable in solution, making it desirable to prepare the solution at the time of use rather than far in advance of the conditioning. Varying concentrations of the hydroxylamine solutions correspondingly varies the amount of chemical modification which the fibers undergo. At room temperatures a 20 percent water solution of NH_2OH which is allowed to contact the collagen for about 10 hours so modifies the fibers that about 10 moles of hydrazides are introduced per 10^5 gms. of collagen and about 10 moles of amides are removed from a like quantity of collagen. Increasing the hydroxylamine concentrations to about 70 percent by weight under like conditions causes about 24 moles of hydroxamates to be introduced into the fibers per 10^5 gms. of collagen, about 15 moles of amides to be removed, and about 12 moles of arginine to be converted to ornithine.

Depending on reaction conditions, the fibers of our invention consist of collagen fibers having the general physical properties of collagen and essentially consisting of collagen fibers containing about 10 to 46 moles of hydroxamates per 10^5 gms. of collagen, 10 to 24 moles of amides per 10^5 gms. of collagen, less than that contained in native collagen, and having 1 to 24 moles of arginine converted to ornithine.

Although we may use a temperature of from about 0 to 60° C., we prefer for convenience to use room temperatures. Lower temperatures usually require somewhat longer conditioning times and these lower temperatures are of no particular advantage. Higher tempera-