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(54) Title: PROCESS FOR TANNING LEATHERS WITH TRIAZINE DERIVATIVES

(57) Abstract: Process for tanning leathers with triazine derivatives comprising at least the steps of transforming a raw animal skin into a de-calcined leather, placing the de-calcined leather in a container with water at room temperature, rotating said container, adding a triazine derivative, dissolved in water, in a concentration ranging between 5.5% and 22%, with respect to the pelt weight, or adding water soluble condensing agents, and draining and washing in water.

PROCESS FOR TANNING LEATHERS WITH TRIAZINE DERIVATIVES

The present invention relates to a process for treating high molecular weight proteins, particularly proteins deriving from the rough skin of animals, which allows to raise their hydrothermal stability and their resistance to rot, thus obtaining a tanned leather.

More specifically, the invention describes a process for tanning leathers with triazine derivatives, in particular with dimetossitriazin-N-metilmorfolinio salts, such as, for example, the 4-(4,6-dimethoxy-1,3,5-triazin-2-il)-4-metilmorfolinio chloride (DMTMM).

The tanning process of leathers consists of different steps, in order to transform the animal skin, which is easily subjected to bacterial attacks, into a stable and resistant to rot material. According to a general known tanning process, the rough skin is normally renewed, calcined, shaved, de-calcined and soaked. The combination of said processes, traditionally referred to as the "Riviera method", allows to remove unwanted substances (dirt, grease, blood, interfibrillary proteins, hyaluronic acid, etc.) from the skin and to open the dermal fibers in a controlled way. The only component of the skin which is useful for performing a tanning operation is the collagen, i.e. the protein constituting the fibrous reticulum of the leather.

According to the tanning agent which is used, the de-calcined and soaked skin is normally subjected to a specific treatment before the tanning phase, in order to minimize the reactivity of the collagen-tanning agent and to support the penetration of said agent through the whole thickness of the leather. In some substantial cases said treatment consists in an

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acidification, technically called "pickling", which is made by using an electrolyte which raises the osmotic pressure of the bath. Said effect is performed in order to remove the swelling of the skin which would

5   otherwise occur together with the lowering of the pH below the isoelectric point of collagen (the "pickling" treatment is carried out by using the formic acid and the sulfuric acid as pH regulators and the sodium chloride as an osmotic electrolyte).

10   When the leather is impregnated with tanning agent in conditions of low reactivity, it is possible to change the pH, thus obtaining the fixing of the tanning agent to the collagen matrix. It is very important that a molecule of the tanning agent has, in addition to a

15   high affinity towards the organic substrate, also a good ability to penetrate into the fibers of the skin, in order to avoid wrinkling, over-tanning or other unwanted effects.

In the case of chrome tanning, after a suitable

20   pickling process, the chromium salt is added and, once the tanning agent is penetrated into the leather, is the pH of the bath is raised from 2.8 up to 3.8-4.2, thus obtaining the final fixing. The overall duration of the tanning process depends on the type of skin to

25   be treated up to a maximum of 20-24 hours.

In practice, the above values may be subject to slight changes according to the particular formulation and to the characteristics of the leather to be made.

At present there are different types of tanning for

30   leathers; however, those the types of tanning which are of most interest for industry are the following:

a) mineral tanning (almost exclusively performed with basic salts of trivalent chromium; salts of titanium,

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zirconium and aluminum are also used),

b) tanning with aldehydes,

c) tanning with synthetic tannins (syntan),

d) tanning with vegetable tannins (exclusively for sole leather).

Over 85% of the leather produced in the world is made of chrome tanning, due to the high stability to heat, moisture, and to the physical and technical features of the finished product. In particular, the hydrothermal stability is indicated by the gelatinization temperature, T_g, which in this case easily exceeds 100°C. However, the leathers tanned with chrome are characterized by an intrinsic blue-gray coloration due to the presence of trivalent chromium which is incorporated in the fibers and which adversely affects the brightness of the dyes and consequently limits the range of colors.

By using the tanning with aldehydes it is possible to obtain leathers with good performances but rather spongy, with low fullness and characterized by a yellowish color. For these and other reasons, the aldehydes are very rarely used as the sole tanning agent, but are suitably combined with other substances thus obtaining a mixed tanning.

The synthetic tannins, while presenting significant advantages over natural tannins, give rise to a leather characterized by both a low gelatinization temperature and a reduced dyeability. The tanning with synthetic tannins also requires, as well as the natural tannins, high amounts of the tanning agent; therefore, the synthetic tannins, as well as the aldehydes, are almost always employed for obtaining a mixed tanning.

The vegetable tannins, when used as first-tanning

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agents, give to the leather a high fullness and are used almost always for producing soles and heavy leathers.

A common feature of the known tanning agents is to interact with the collagen of the skin/leather, so as to permanently remain inside its structure. For this reason, the methods of tanning listed above have important critical aspects both from an environmental point of view and from a toxicologically point of view, mainly due to the disposal of waste (both solid and liquid) and to the presence of substances which are harmful to health inside the leather. In particular, it is known that under certain conditions it is possible to have, in chrome-tanned leathers, a leakage of hexavalent chromium, which is a noxious and carcinogenic chemical substance. Even the aldehyde tanning (THPS, oxazolidine I and II) by the time release appreciable amounts of formaldehyde (a carcinogen substance), while the synthetic tannins can release formaldehyde and phenol (cytotoxic substances). Therefore, in recent years, both as a result of environmental regulations and health protection and to improve awareness by consumers, is increasingly felt the need for alternative tanning agents.

In theory the chrome tanning raises a particular interest because of the excellent features that causes to the leather. In the search for new tanning molecules, it is therefore useful to consider the mechanisms of said chrome tanning in an attempt to reproduce them with other chemical substances. Specifically, the transformation of the collagen which is performed during the chrome tanning is due to the reaction between polynuclear complexes of trivalent

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chromium and carboxyl groups of the collagen chain, with the formation of chemical bonds having a partially covalent character that interconnect in a very stable way different sites of the molecules of collagen.

5   The force and the thermodynamics inertia of the chemical bond is one of the reasons why the chrome tanning gives the leather the higher gelatinization temperatures (Tg).

In practice, a chemical substance has best tanning
10   properties as the number of bridge covalent bonds, which are formed between adjacent chains of collagen, increases. That's why the tanning agent (or a derivative product in situ) becomes an integral part of the collagen matrix and remains embedded inside the
15   leather at the end of the tanning reaction.

However, the terminal and lateral functional groups of collagen that are usually involved in the tanning reaction may react together and form stable bonds even without the use of a tanning molecule. In fact,
20   exploiting the reactivity of the carboxy and amino functionality of the collagen, it is possible to generate a high degree of intramolecular cross-linking through the formation of amide bonds. Consequently, the search for new chemical species that stabilize the
25   collagen may also extend to condensing agents which do not remain permanently incorporated inside the collagen matrix.

A wide range of studies on the formation of amide or ester, which are obtained, respectively, from the
30   condensation between a carboxylic acid and an amine or an alcohol, are also known; said products are of great commercial interest as are often used in the field of drugs, polymers, biomolecules, etc.

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Thanks to their acid-base characteristics, a carboxylic acid (RCOOH) and an amine (R'NH2) initially react to form the corresponding quaternary ammonium salt, according to the formula:

$$R\text{-}COOH + R'\text{-}NH_2 \rightarrow R\text{-}COO\text{-} \ +H_3N\text{-}R'$$
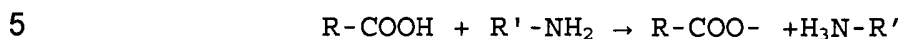
The subsequent formation of the amide bond requires the elimination of a water molecule, as shown in the following equation:

$$R\text{-}COO\text{-} \ +H_3N\text{-}R' \leftrightarrow R\text{-}CONH\text{-}R' + H_2O$$
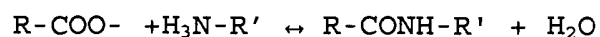
An activating agent that leads to the formation of a group including acylchloride, acilazide, acilimidazolo, anhydride, etc. is generally employed in order to obtain the amide (or ester).

A method which makes use of carbodiimides is widely employed for the condensation of amino acids with formation of peptide bonds. Carbodiimides are organic molecules having basic characteristics thanks to the presence of two nitrogen atoms, which react with an acid, thus generating the O-acilisourea, i.e. an intermediate reactive substance which, by using an amine, gives the desired peptide bond through ammonolysis.

One of carbodiimides most used for this purpose is the dicyclohexylcarbodiimide (DCC), which gives rise to the formation of N,N'-dicyclohexylurea (DCU) as a co-product of the reaction, which must be removed by purification at the end of the synthesis.

Until a short time ago, the coupling reactions between amines and carboxylic acids in aqueous solvent were only conducted in the presence of water-soluble carbodiimides, such as the 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC), which gives the formation of the 1-(3-(dimethylamino)

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propyl)-3-etilurea, which is in turn water-soluble and therefore easily removable at the end of the reaction. A considerable disadvantage in the use of EDC is constituted by its poor stability, which requires storage at low temperature (ca. -20°C).

In 1996 Luyn et al. have reported a first example of the use of EDC in the presence of N-hydroxysuccinimide (NHS) as an activator for the cross-linking of lyophilized collagen, thus obtaining, at the best reaction conditions, a maximum value of Tg=82°C. However, in order to obtain the maximum value of Tg, high concentrations of reagents are required (up to five times the moles of EDC with respect to the moles of COOH which are present in the collagen).

Therefore, the EDC/NHS system is generally employed as a co-reagent in presence of macromolecules with a high number of amine groups capable of reacting with the carboxyl groups of collagen by increasing the cross-linking degree and consequently the Tg with respect to what is obtained only by using the EDC/NHS system. Normally dendritic amines are used (synthetic polymers obtained by convergent or divergent reaction), which, by reacting with the carboxyl groups of collagen, can be inserted permanently within the collagen structure by changing its properties in an irreversible way.

In recent years, dendrimers have received considerable interest because of their possible use in the medical field as drug delivery systems.

Repeating cyclically a given sequence of reactions, it is possible to obtain subsequent generations of dendrimers with increasing molecular weight and number of terminal functional groups (G0, G1, G2, etc.).

However, the cross-linking reaction between the

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collagen and dendrimers requires the use of high
amounts of EDC/NHS so as to make this procedure of
little practical interest except that for specific
medical applications, such as the reconstruction of
corneal tissue, cartilage, skin, etc.

Among the known various condensing agents, the 2-
chloro-4,6-dimethoxy-1,3,5-triazine (CDMT) is employed
as an alternative to carbodiimidi, thus allowing to
obtain the condensation of a carboxylic acid with an
amine in bland conditions and to easily recover the
product. More recently, the synthesis of the 4-(4,6-
dimethoxy-1,3,5-triazin-2-yl)-4-metilmorfolinio
chloride (DMTMM) has been performed and said substance,
unlike the CDMT, can also be used in watery
environment.

A further advantage of the DMTMM is constituted by the
possibility of being regenerated at the end of the
reaction. Indeed, the final co-product of the reaction
[2-hydroxy-4,6-dimethoxy-1,3,5-triazine (DMT-OH)] is
very soluble in an aqueous phase and may be removed
from the mother liquor for concentration. One study
reports that about 70% of DMT-OH can be recovered as
described and converted into DMTMM.

Moreover, the DMTMM, as well as the EDC/NHS, has found
wide use in recent years in the medical field for the
reconstruction of tissues and for the synthesis of
oligonucleotides that are used in the medical field.

It is important to underline that both the EDC/NHS and
the DMTMM allow the condensation but they do not remain
chemically bonded to the substrate at the end of the
reaction.

In this context it is included the solution according
to the present invention, which aims to treat proteins

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of high molecular weight so as to give a high
hydrothermal stability and high resistance against the
putrefaction.

These and other results are obtained according to the
present invention by proposing a set of operating
conditions for obtaining, starting from the rough
animal skin, a tanned leather with a high temperature
of gelatinization in the presence of triazine
derivatives and, in particular, in the presence of a
well-determined derivative substance. The stabilization
of the structure is due to the increase of the cross-
linking degree of the collagen, thanks to the formation
of new amide bonds, which is carried out under mild
conditions of reaction and without the incorporation of
the reagent within the protein structure.

An object of the present invention is therefore to
provide a process for tanning leathers with the salts
of dimetossitriazin-N-metilmorfolinio and in particular
with the 4-(4,6-dimethoxy-1,3,5-triazin-2-)-4-
metilmorfolinio chloride, which allows to obtain the
previously described technical results.

A further object of the invention is to provide a
process for tanning leathers which can be performed
with substantially reduced cost with respect to the
known tanning methods.

Another object of the invention is to provide a process
for tanning leathers which is simple and safe and which
provides for an easy standardization.

Therefore, it is an object of the present invention to
provide for a process for tanning leathers by using the
triazine derivatives according to the enclosed claim 1.

It is clear the effectiveness of the process of the
present invention, which allows to obtain leathers with

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high resistance to rot, high hydrothermal stability and
excellent dyeability thanks to the characteristic white
color, due to the absence of intrinsic colors. The
method of tanning implemented according to the present
5   invention does not have problems about the disposal of
solid waste and does not use substances harmful to
health in the finished product, such as carcinogens
and/or cytotoxic substances.

In fact, an important feature of this process is the
10 use of a tanning reagent, which is not retained within
the collagen support, whose chemical composition
remains unchanged.

The invention will be described below for illustrative,
but not limitative, purpose and with particular
15 reference to some illustrative examples.

Example 1. DMTMM WITHOUT pH CONTROL.

In a beaker of 50 ml containing a solution of 42 ÷ 166
mg (from 0.15 to 0.60 mmol) of DMTMM and 25 mL of
distilled water, 250 mg (corresponding to 0.3 mmol of
20 carboxyl groups) of collagen powder are added. The
becker is placed under stirring and the pH is monitored
every 60 minutes. After 4 hours the suspension is
filtered on Buchner and washed with 50 ml of distilled
water. The collagen thus treated is then analyzed
25 through DSC. The results are the following:

$$0.15 \text{ mmol} \rightarrow Tg = 85°C$$

$$0.30 \text{ mmol} \rightarrow Tg = 84°C$$

$$0.60 \text{ mmol} \rightarrow Tg = 81°C$$

Example 2. DMTMM WITH pH CONTROL AND pH=5.5.

30 In a beaker of 50 ml containing a solution of 42 mg
(0.15 mmol) of DMTMM, 20 ml of distilled water and 5 ml
of buffer sodium acetate/acetic acid (pH = 5.5), 250 mg
(corresponding to 0.3 mmol of carboxyl groups) of

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collagen powder are added. The system is placed under
stirring and the pH is monitored every 30 minutes and
corrected if necessary with addition of buffer or
acetic acid in a range from 5.3 to 5.9. After 4 hours
the suspension is filtered on Buchner and washed with
50 ml of distilled water. The collagen thus treated is
then analyzed through DSC. Results:

Tg = 72-75°C.

EXAMPLE 3. EDC/NHS WITH pH CONTROL AND pH = 5.5.

In a beaker of 50 ml containing a solution of 115 mg
(0.6 mmol) of EDC, 69 mg (0.6 mmol) of NHS and 25 ml of
distilled water, 250 mg (corresponding to 0.3 mmol of
carboxyl groups) of collagen powder are added. The
system is placed under stirring and the pH is monitored
every 30 minutes and possibly corrected with HCl/NaOH.
After 4 hours the suspension is filtered and washed
with 50 ml of distilled water. The collagen thus
treated is then analyzed through DSC. Results:

Tg = 73°C.

EXAMPLE 4. DMTMM WITH NO pH CONTROL AND DENDRIMERS.

In a beaker of 50 ml containing a solution of 42 mg
(0.15 mmol) of DMTMM and 25 ml of distilled water, 250
mg (corresponding to 0.3 mmol of carboxyl groups) of
collagen powder and 5 ml of an aqueous solution of a
dendrimer, corresponding to 0.3 mmol of amine groups
(in case of dendrimer G.0 0.075 mmol, while in case of
dendrimer G.1 0.0375 mmol) are added. The system is
placed under stirring and the pH is monitored every 60
minutes. After 4 hours the suspension is filtered on
Buchner and washed with 50 ml of distilled water. The
collagen thus treated is then analyzed through DSC. The
results obtained with dendrimers are reported below:

1) with 0.15 mmol of DMTMM: (no pH control)

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2G0: Tg = 68°C

3G0: Tg = 67°C

4G0: Tg = 67°C

3G1: Tg = 65°C

5   2) with 0.30 mmol of DMTMM: (no pH control)

4G0: Tg = 70°C on wet sample

4G0: Tg = 82°C on dry sample

3) with 0.30 mmol of DMTMM: (pH = 5.5)

4G0: Tg = 75°C

10   EXAMPLE 5. EDC/NHS WITH pH CONTROL AND DENDRIMERS.

In a beaker of 50 ml containing a solution of 115 mg (0.6 mmol) of EDC, 69 mg (0.6 mmol) of NHS and 25 ml of distilled water, 250 mg (corresponding to 0.3 mmol of carboxyl groups) of collagen powder and 5 ml of a

15   solution of dendrimer corresponding to 0.3 mmoles of amine groups (dendrimer G.0: 0,075 mmol) are added. The system is placed under stirring and the pH is monitored every 30 minutes and possibly corrected with HCl/NaOH. After 4 hours the suspension is filtered on Buchner and

20   washed with 50 ml of distilled water. The collagen thus treated is then analyzed through DSC. Results:

2G0: Tg = 79°C

3G0: Tg = 77°C

4G0: Tg = 85°C

25   EXAMPLE 6. TEST ON LEATHER SAMPLES.

A piece of leather of about 100 g revived and calcined/decalcined in accordance with normal industry practices, it is treated as follows according to the chosen tanning system.

30   WITH DMTMM.

A piece of decalcined leather of about 100 g is placed in a drum containing 100 ml of water at room temperature. The system is rotated and then the DMTMM

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is added (at different concentrations, from 22% to 5.5%, with respect to the pelt weight); the DMTMM is dissolved in 200 ml of water. No control of pH or temperature. After 4 hours, the bath is drained and the system is washed 2 times with water. Result:

Tg = 83°C.

WITH EDC/NHS.

A piece of decalcined leather of about 100 g is placed in a drum containing 100 ml of water at room temperature. The system is rotated and the pH is controlled with formic acid/ammonia in a range between 5.0 and 5.5. Then, EDC and NHS are added (14% EDC and 8% NHS, with respect to the pelt weight); EDC and NHS are dissolved in 200 ml of water. The system is rotated and the pH is measured and, if necessary, is corrected at regular intervals of 30 minutes. After 4 hours the bath is drained and the system is washed 2 times with water. Result:

Tg = 84°C.

The leather samples are then pressed and split, re-tanned and fattened according to the industrial practice.

The above description makes clear the technical characteristics of the process for tanning leathers with triazine derivatives, as well as clear are the related advantages.

It should be noted, finally, that although the present invention has been described for illustrative but not limitative purposes, according to preferred embodiments, variations and/or modifications can be made by the man skilled in the art without departing from the relevant scope as defined by the appended claims.

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CLAIMS

1. Process for tanning leathers with triazine derivatives comprising at least the following steps:
- converting a raw animal skin into a calcium-removed skin, eliminating unwanted substances and controlled opening of the dermal fibers of said skin;
- placing the calcium-removed skin inside a container with water at room temperature;
- rotating said container;
- adding a water-soluble triazine derivative in a concentration ranging between 5.5% and 22%;
- draining and washing the skin with water.

2. Process according to claim 1, characterized in that said triazine derivative is formed by salts of dimetossitriazin-N-metilmorfolinio.

3. Process according to claim 2, characterized in that said salts include the 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-metilmorfolinio chloride (DMTMM).

4. Process for tanning leathers with triazine derivatives comprising at least the following steps:
- converting a raw animal skin into a calcium-removed skin and eliminating unwanted substances and controlled opening of the dermal fibers of said skin;
- placing the calcium-removed skin inside a container with water at room temperature;
- rotating said container;
- adding water-soluble condensing agents in a concentration ranging from 5.5% to 22% wt.;
- further rotating said container;
- measuring and correcting the pH at constant time intervals;
- draining and washing the skin with water.

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5. Process according to claim 4, characterized in that said condensing agents are constituted by water-soluble carbodiimides.

6. Process according to claim 5, characterized in that said water-soluble carbodiimides are constituted by 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC).

7. Process according to claim 6, characterized in that said 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC) is added in the presence of N-hydroxysuccinimide (NHS) as activator for the cross-linking of collagen.