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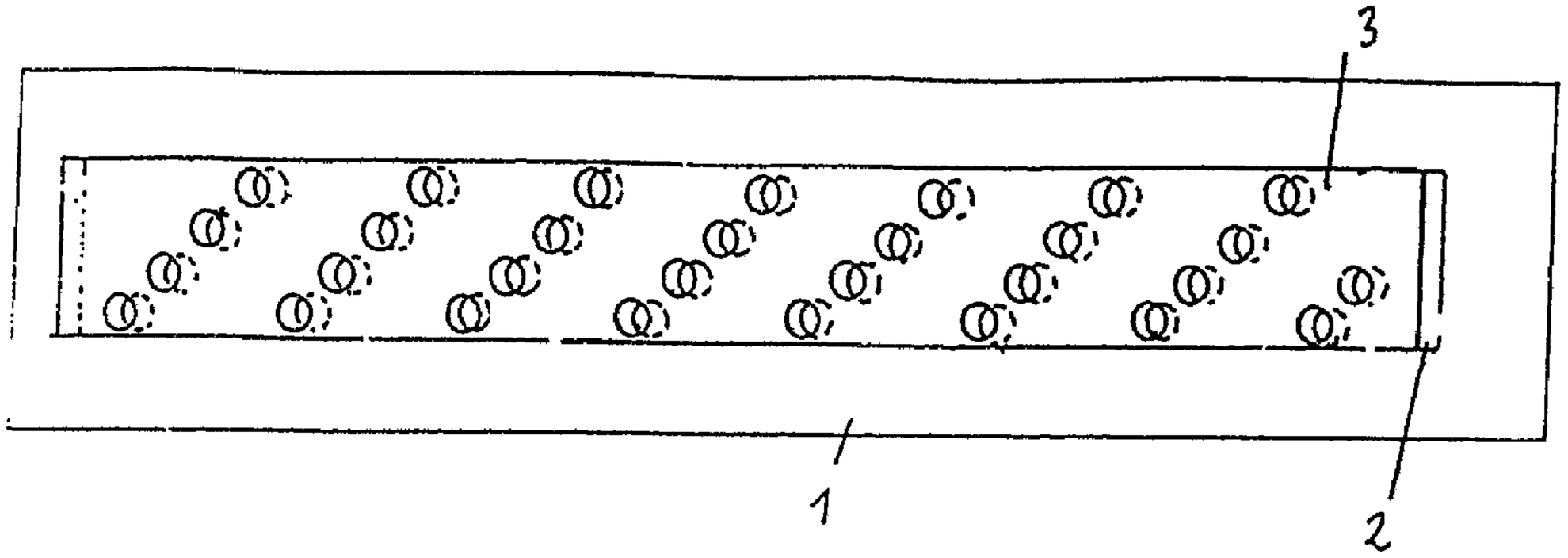
(54) Titre : DISPOSITIF POUR L'APPLICATION EGALE D'UNE SUSPENSION A UN SUPPORT DE BASE DE COLLAGENE

(54) Title: A DEVICE FOR THE EVEN APPLICATION OF A SUSPENSION TO A COLLAGEN CARRIER



(57) Abrégé/Abstract:
A process for the production of a material for sealing and healing wounds comprises the even application of a suspension to a collagen carrier. An elongated container, into which the suspension is filled, is provided with a base frame and a set of two perforated plates as its bottom. The upper plate is movable and is continuously moved back and forth during the process at a right angle to the transport direction of the collagen carrier, which allows the suspension to drip on the collagen carrier which is transported underneath the container.

ABSTRACT

A process for the production of a material for sealing and healing wounds comprises the even application of a suspension to a collagen carrier. An elongated container, into which the suspension is filled, is provided with a base frame and a set of two perforated plates as its bottom. The upper plate is movable and is continuously moved back and forth during the process at a right angle to the transport direction of the collagen carrier, which allows the suspension to drip on the collagen carrier which is transported underneath the container.

A device for the even application of a suspension to a collagen carrier

The invention relates to a device for the even application of a suspension to a collagen carrier for the production of a material for sealing and healing wounds.

A material for sealing and healing wounds which comprises a collagen carrier coated with a fibrin component, a thrombin component, such as calcium ions, protease inhibitors or heparin antagonists, is known from US 4,453,939.

To prepare this material, the individual components or additives are suspended in an organic solvent, e.g. ethanol, and subsequently applied to a collagen carrier, e.g. by means of spraying.

In doing this several problems arise, because the suspension to be applied is difficult to handle. For example, the nozzle used usually for these purposes clog immediatly. Lingnial air nozzles permit the use of a larger diameter, but even in this case, only nozzles with the largest diameter available enable working with a sufficient lack of trouble. However these nozzles show a decisive disadvantage. The indistinct definition of the exiting stream does not an even layer of the suspension but creates a trapezoidal coating profile on the collagen carrier. This leads to considerable losses of collagen carrier and valuable suspension at the edges.

A device for applying a liquid film to a fabric web according to the pouring-out principle is known from EP-A 472 050. By means of individual partitions for liquid which are located directly next to one another, this device achieves a forced distribution of the liquid form a feed opening to a number of outflow openings. The liquid is distributed in the form of a family tree, i.e step by step from one opening to two, four, eight, sixteen etc, outflow openings. This device is not suitable for the even distribution of a suspension comprsing fibrinogen and thrombin components, as the several divisions of the liquid stream cause conglutination and clogging of the partitions by the suspension; furthermore, this conglutination and clogging occurs to a greater extent then when nozzles are used.

The problem solved by the present invention was therefore to prevent the disadvantages of the previosly known methods.

Brief Description of the Drawings

Further aspects and advantages of the present invention will become apparent from the following description, taken together with the accompanying drawings, in which:

Figure 1 is a top plan view illustrating a device according to the present invention for the even application of a suspension to a collagen carrier;

Figure 2 is a schematic diagram showing the size and positioning of the flow-thorough holes in the device according to the present invention of Example 1;

Figure 3 is a graph showing the profile of the fibrinogen coating, at a right angle to the direction of transport, produced by the device of Example 1; and

Figure 4 is a graph showing the profile of the fibrinogen coating, at a right angle to the direction of transport, produced by a previously known spraying technique.

The object of the invention is therefore a device for the even application of a suspension to a collagen carrier for the production of a material for sealing and healing wound, comprising a container into which the suspension is filled the bottom of said container consisting of a base frame (1) and a perforated base plate (2) whereby a moveable perforated plate (3) is mounted directly above the perforated base plate (2).

A further object of the invention is therefore a process for the production of a material for sealing and healing wounds, comprising: filling a suspension into an elongated container, the elongated container having a base frame and two perforated plates forming a bottom of the elongated container, the two perforated plates including an upper plate and a lower plate, and the upper plate being movable relative to the lower plate; transporting a collagen carrier below the elongated container in a transport direction; and continuously moving the upper plate back and forth in a direction that is at a right angle to the transport direction so as to allow the suspension to drip on to the collagen carrier being transported below the elongated container, whereby the suspension is evenly applied to the collagen carrier.

The container is provided with a rectangular perforated base plate (base plate (2)) which is surrounded by the base frame (1) and upon which lateral boundary walls rest. A second perforated plate is mounted directly above the perforated base plate (2) and this plate can be moved back and forth inside the container: movable perforated plate (3).

The suspension to be filled into container comprises a fibrinogen component, a thrombin component, aprotinin (which acts as protease inhibitor) and other additives such as calcium ions or heparin antagonists in alcohol such as ethanol, n- or I- propanol or n- or I-butanol. This suspension is used for the production of a material for sealing and healing wounds and for other medical uses. For this reason, the device, especially the perforated plates, must be

constructed of a material which is abrasion-resistant and which cannot react with the suspensions. Suitable materials would be for example high grade steel or titanium. The lateral boundary walls can also be constructed of glass or plexiglass, which makes it possible to easily observe the suspension in the container.

Both perforated plates are provided with one or more rows of holes, whereby the flow-through holes in the rows are arranged at equal distances. Preferably the plates are provided with several rows of holes.

The diameter of the flow through holes chosen must be large enough to prevent the suspension from clogging them.

The ratio of the flow-through holes' diameter to that of the largest particle in the suspension amounts to approximately 5 : 1 to 50 : 1, preferably 7.5 : 1 to 40 : 1 and most preferably 10 : 1 to 30 : 1.

The largest particles present in the suspension possesses a diameter of approximately 0.1 mm to 0.2 mm.

In a perferable embodiment of the device according to the invention the diameter of the flow-through holes is approximately 2 to 3 mm.

The center of the flow-through holes are preferably located at a distance or approximately 2 to 8 mm, especially perferabyl at a distance of 3- 4.5 mm from the face of the coating and at right angle to it.
Depending on the number of rows, the distance between the neighboring holes in a row can measure up th 16 mm and more.

In applying the suspension to a collagen carrier, the previously homogenized suspension is pumped into the container at a constant speed, whereby the movable perforated plate lies on top of the perforated base plate in the beginning in such a way as to close the flow-through holes. The seal should be as efficient as possible and can optionally be assisted by bearing weights being placed on top of the movable perforated plate.

As soon as the suspension in the container has reached the stationary level corresponding to the given pumping speed the coating apparatus is put into operation. This causes the movable perforated plate to move back and forth over the stationary perforated plate. The two perforated plates coincide at a certain position (preferably in the middle between the two stationary points at which the movably perforated plate changes direction) and the suspension can drip onto the collagen carrier, which is passed under the coating apparatus on a conveyer belt.

The level of the suspension in the coating apparatus remains constant during this process provided that additional suspension is pumped in.

The varying excursional distances of the movable perforated plate allows a wide range for setting the ratio of the intervalls of closure and opening. This makes it possible th choose hole diameters of a size with which no complications result and, at the same time, limit the drip speed.

In consideration of the arrangement of the holes and the speed of the conveyor belt, a distribution pattern of the holes can be achieved with which the drops form the corners of equilateral triangles, which correspond to layer of spheres packed as tightly as possible.

The perforated plate preferably moves at a right angle to the direction of the conveyor belt.
The back and forth movement of the movable perforated plate simultaneously ensures that the suspension remains homogenous, so that an even distribution of the components is achieved on the collagen carrier.. Mixing can be assisted optionally by means of additional arrangements on the movable perforated plate or by a mixer.

Another embodiment of the invention is that the container into which the suspension is filled is constructed as a tube or semi-tube provided with holes into which a movable perforated tube or semi-tube is mounted. Moving the inner tube causes periodically opening and closing of the holes, thus achieving the desired effect.

With the aid of the device according to the invention, applying an exactly defined breadth of the suspension is possible without loss of suspension or collagen carrier at the edge.

The profile of the coating achieved after evaporation of the suspension medium is not trapezoidal (as it is using known spraying techniques) bit rectangular.

A comparative test, in which the loss at the edge resulting when using previously known spraying technique, in which an lignial air nozzle is used, is compared to the loss resulting with the device according to the invention, shows that more than five times more suspension is lost with the lignial air nozzle than with the device according to the invention.
A relatively small batch was used in this test. The ratio increases correspondingly as the batch size increases. A loss of suspension during application with the device according to the invention occurs only with the residual volume of suspension remaining in the container after pumping ceases.

Example 1:

In a container provided with a perforated base plate and a movable perforated plate with the following dimensions:

Breadth: 450 mm
Depth: 12 mm
Number of rows of holes: 2
Diameter of flow through holes: 2 mm
Distance between the centers of the two flow through holes located in one row: 8 mm
Distance between the rows of holes: 6.9 mm

(The arrangement of the flow-through holes is shown in fig. 2).

in which the perforated plates were closed, a suspension of 55 mg/ml of fibrinogen 20 IU/ml of thrombin and 0.71 Ph. Eur. U/ml of aprotinin in ethanol was pumped at a speed of 450 ml/min until the stationary level of the liquid of 50 mm was reached. At that point, the movable perforated plate was put into motion at 400 cycles/min, whereby the excursion measured 6 mm in both directions.
A breadth of 450 mm of the suspension was then dripped onto a collagen sponge measuring 5 mm in height which was being transported underneath the container by a conveyor belt at a speed of 1 m/min and at a right angle to the movement of the movable perforated plate. After evaporation of the suspension liquid the collagen carrier was coated with approximately 5.5 mg/cm2 of fibrinogen, 2 IU/cm2 of thrombin and 0,071Ph.Eur.U./cm2 of aprotinin.
The loss at the edge was less than 1 %.
The profile of the coating at a right angle to the direction of transport is shown in fig.3.

Comparative Example:

A breadth of 450 mm of a suspension with the same composition was again applied to a collagen carrier which was transported on a conveyor belt. Fig 4 shows the best result achieved in numerous tests with various lignial air nozzles.

In this example, a nozzle combination from Spraying systems Inc., which features a turnaround surface, was used. The best sample was chosen from numerous examples of the same model.

The profile of the coating at a right angle to the direction of transport is shown in fig. 4 , in which the distribution of fibrinogen at a right angle to the direction of the conveyor belt is shown. Even under these conditions, the loss of suspension falling from both sides still amounts to approximately 20 %.

The embodiments of the invention for which an exclusive property or privilege is claimed are defined as follows:

1. A process for the production of a material for sealing and healing wounds, comprising:

filling a suspension into an elongated container, the elongated container having a base frame and two perforated plates forming a bottom of the elongated container, the two perforated plates including an upper plate and a lower plate, and the upper plate being movable relative to the lower plate;

transporting a collagen carrier below the elongated container in a transport direction; and

continuously moving the upper plate back and forth in a direction that is at a right angle to the transport direction so as to allow the suspension to drip on to the collagen carrier being transported below the elongated container, whereby the suspension is evenly applied to the collagen carrier.

2. The process of claim 1, wherein:

said step of transporting and said step of continuously moving the upper plate back and forth occur simultaneously.

3. The process of any one of claims 1 or 2, wherein said step of continuously moving further comprises regulating the flow rate of the suspension by setting a deflection distance of the upper plate.

4. The process of any one of claims 1 to 3, wherein the two perforated plates are made from a material selected from the group consisting of steel and titanium.

5. The process of any one of claims 1 to 4, wherein the base frame has lateral boundary walls that are made of a transparent material.

6. The process of any one of claims 1 to 5, wherein each of the perforated plates comprise at least one row of holes arranged at equal distances with respect to each other.

7. The process of any one of claims 1 to 6, wherein the suspension comprises particles therein and the ratio of the diameter of a flow through holes in said two perforated plates to a largest particle is from 5:1 to 50:1.

8. The process of claim 7, wherein the ratio is 7.5:1 to 40:1.

9. The process of claim 8, wherein the ratio is 10:1 to 30:1.

10. The process of any one of claims 1 to 9, wherein said step of filling comprises pumping the suspension into the elongated container at a constant speed with perforations in the two perforated plates being out of alignment such that the elongated container is closed, and wherein said steps of transporting and continuously moving are begun when the suspension in the elongated container has reached a set level.

11. The process of claim 10, wherein the level of suspension is maintained constant during said steps of transporting and continuously moving.

12. The process of any one of claims 1 to 11, wherein the suspension comprises a fibrinogen component, a thrombin component and aprotinin, whereby a single layer containing the fibrinogen component and the thrombin component is formed on the collagen carrier during said step of continuously moving.

13. The process of claim 12, wherein the suspension is in alcohol.

14. The process of any one of claims 1 to 11, wherein the suspension comprises an organic solvent.

15. The process of any one of claims 1 to 14, wherein the two perforated plates comprise respective rows of evenly spaced through holes that are alignable and misalignable with each other in the two perforated plates during said step of continuously moving.

16. The process of any one of claims 1 to 15, and further comprising the step of mixing the suspension during said step of continuously moving.

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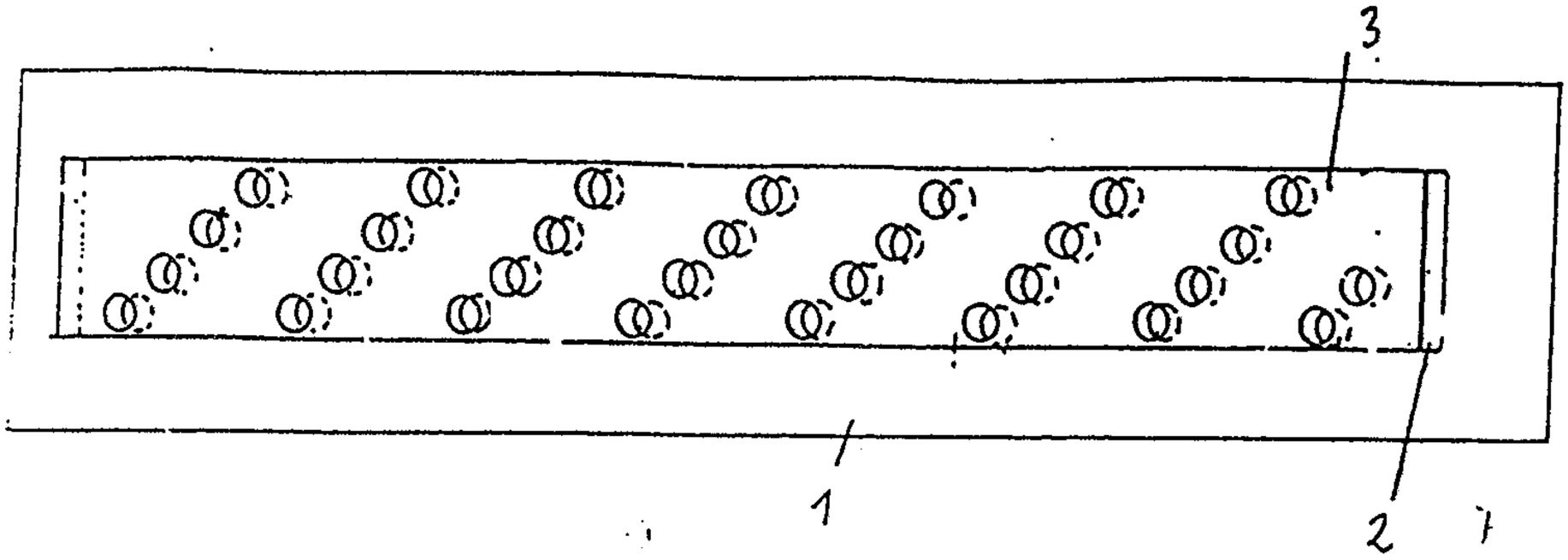

Fig. 1

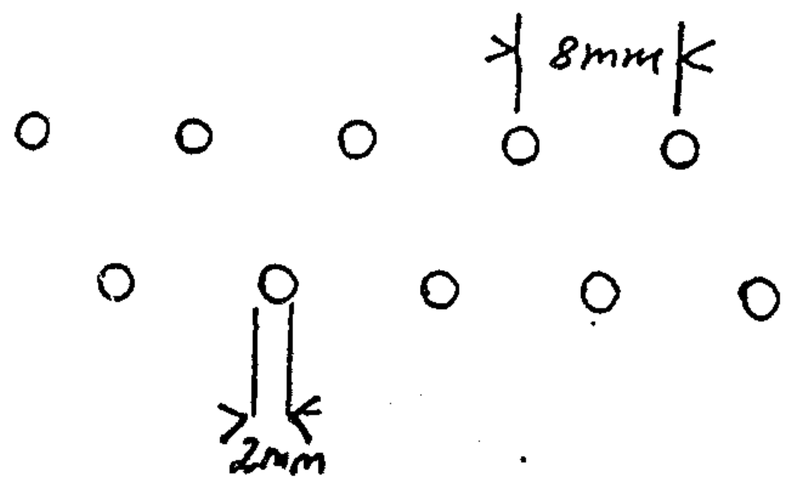

Fig. 2

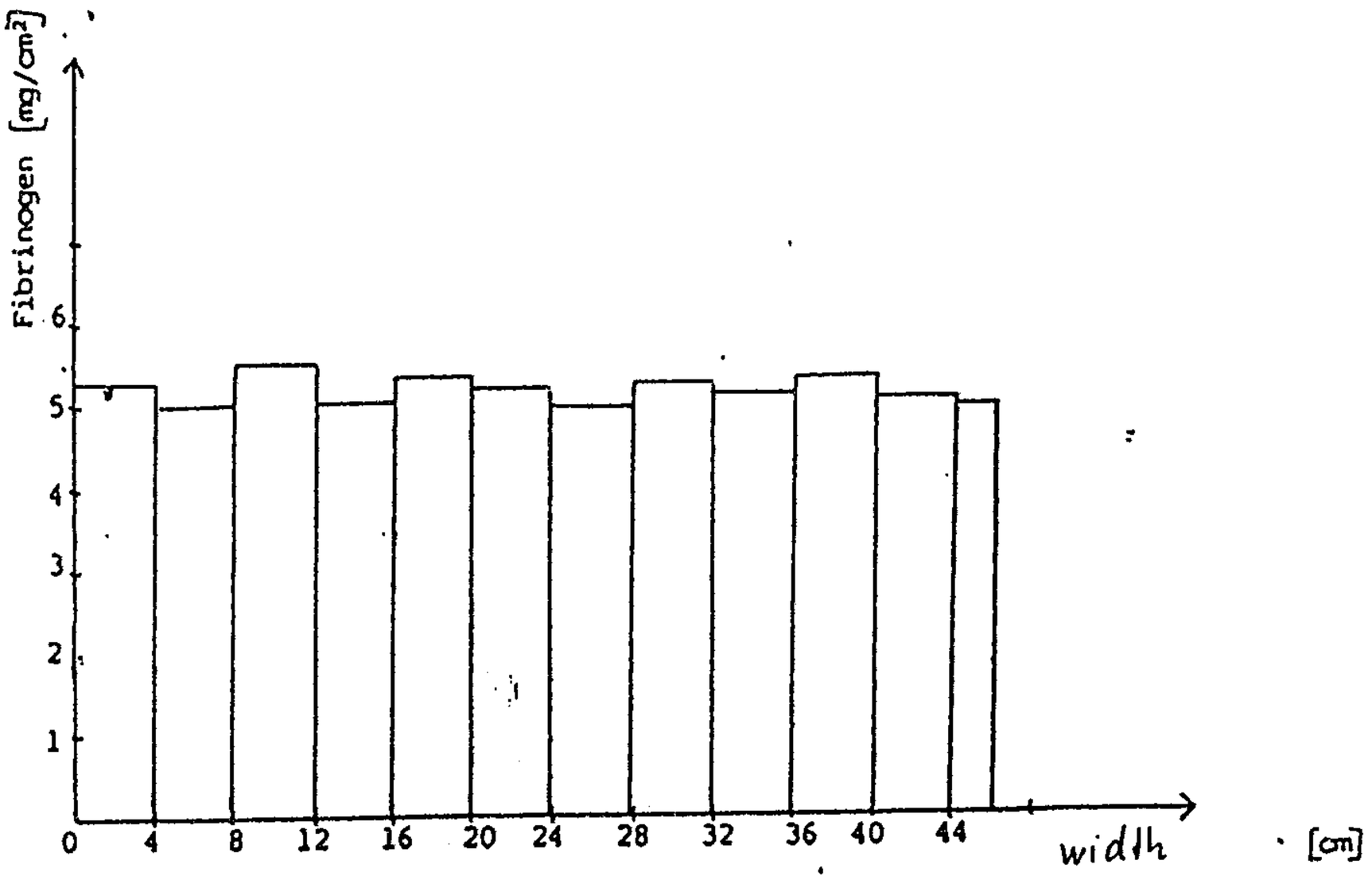
Fibrinogen [mg/cm²]
6
5
4
3
2
1
0
4
8
12
16
20
24
28
32
36
40
44
width
[cm]

Fig. 3

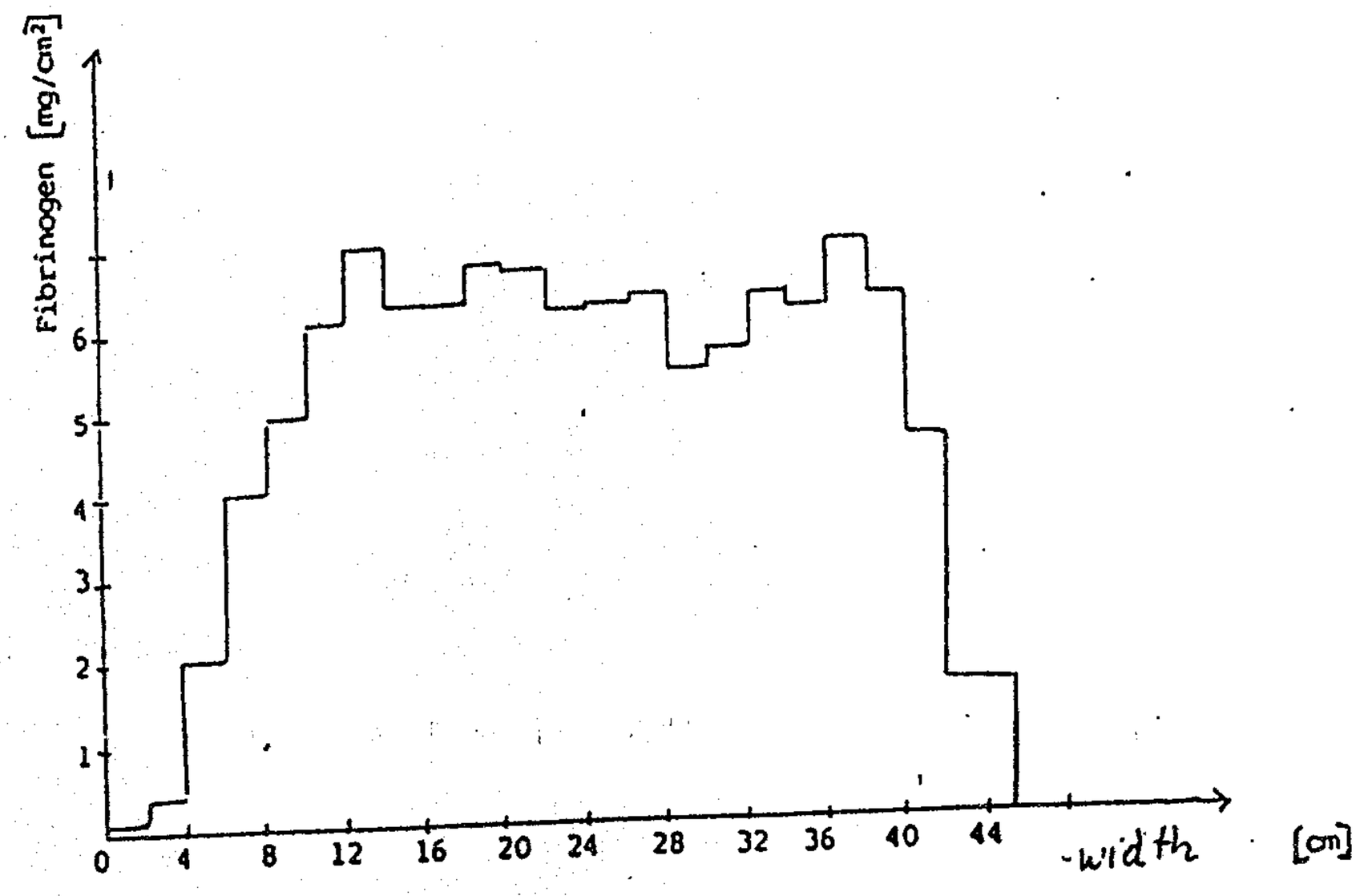
Fibrinogen [mg/cm²]
6
5
4
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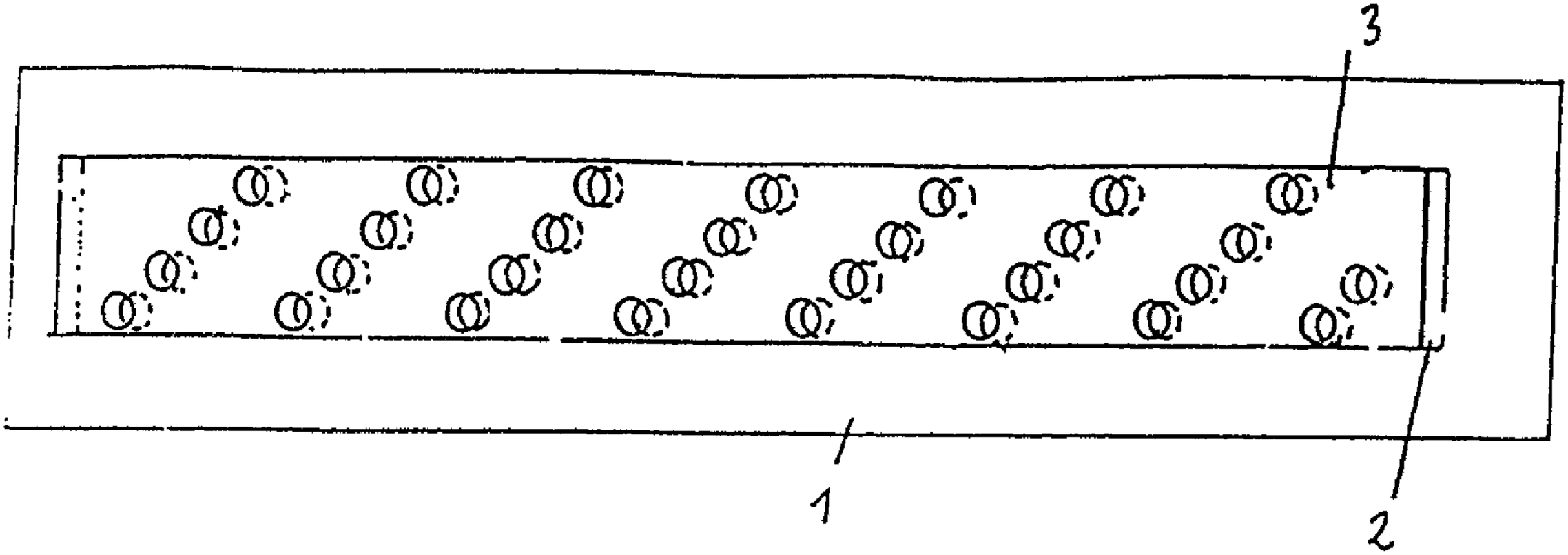
Fig. 4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