Hemostatic Agent Made From Modified Rice Starch

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ABSTRACT - Gelatin hydrogel made from collagen is a common hemostatic agent for topical use especially for neurosurgical operation. The basic properties of the gelatin hydrogel are : 1) It can be absorbed in the living tissue. 2) It is sterile. 3) The ash from burnt hydrogel is less than 2%. 4) The hydrogel can absorb water about 30 times its dry weight. Our objective was to make a topical hemostatic agent from Thai rice, with similar properties as the gelatin hydrogel. Medical grade rice starch was dissolved in hot distilled water and cross-linked with glutaraldehyde. After lyophylization the obtained rice hydrogel was packed and sterilized by gamma ray radiation. A piece of rice hydrogel was placed in an agar plate and burnt under fire and checked for the remaining ash weight. A piece of the rice hydrogel was dissolved in HCl and amylase enzyme. The rice hydrogel was tested for water absorption in distilled water. The Thai rice starch developed into a starch sponge with interconnected porous channels. Burning of the rice hydrogel produced only 0.01 % of ash. The rice hydrogel could be completely dissolved in HCl and amylase solution within 20 min. The material absorbs water 40 times its dry weight and is sterile. The innovative hemostatic rice hydrogel is made in Thailand following the pharmaceutical standards for correct manufacturing, packaging, sterilization and basic laboratory tests. It must undergo further research in animal and clinical trials.

1. Introduction

Gelatin hydrogel made from collagen is a common hemostatic agent for topical use especially for neurosurgical operation.[1] The basic properties of the gelatin hydrogel are: 1) It can be absorbed in the living tissue. 2) It is sterile. 3) The ash from burnt hydrogel is less than 2%. 4) The hydrogel can absorb water about 30 times its dry weight.

In 1945 some researchers tried to make hemostatic hydrogel from corn starch, but it was not practical, because it was too friable and structureless for surgical use.[2,4,5]

Our objective was to make a topical hemostatic agent from Thai rice starch, with similar properties as the gelatin hydrogel.[3]

2. Material and Methods

Manufacturing
Thai rice hydrogel was made by dissolving medical grade rice starch (Erawan Pharmaceutical Research and Laboratory, Thailand) in distilled water to give a 2.5% solution. This mixture is stirred in a flask at about 250 rpm at a temperature of approximately 80 – 100 ^{0}C. Stirring was continued for about 2 hours, until the rice starch solution is homogeneous. 1% Glutaraldehyde (Aldrich) was added to the rice starch solution, for crosslinking the rice starch into a water-insoluble hydrogel. The rice starch hydrogel solution was poured into the polyvinyl plate and left at approximately - 20 ^{0}C to - 40 ^{0}C overnight. The frozen plates were placed in a vacuum oven and sublimed at a pressure below 2.54 mmHg at temperature - 20 ^{0}C until dry. The dried rice sponge was packed in medical grade package (Tyvek, DuPont, Germany) and sterilized by gamma ray radiation (Kendall-Gammatron, Nakornprathom, Thailand).

Laboratory test
Burning
A 50 mg piece of rice hydrogel was burnt and the ash weight on an analytical balance. The test was repeated 10 times.

Sterilization
A piece of sterile rice hydrogel was placed on an agar plate containing full medium, and incubated at 37 ^{0}C for 48 hours. The test was repeated 10 times.

Degradation
A 50 mg piece of rice hydrogel was immersed in distilled water and tenderly squeezed to remove air bubbles, excess water removed using blotting paper. The water-saturated rice hydrogel was transferred into 20 ml of 0.1 N hydrochloric acid and 5 ml of 1% amylase solution was added. The mixture was smoothly shaken at 37 ^{0}C until the rice hydrogel was completely dissolved. The test was repeated 10 times.

Water absorption
A 10 mg piece of rice hydrogel was immersed into distilled water and air bubbles remove by tenderly squeezing. Excess water was removed from the rice hydrogel by using blotting paper. Then the rice hydrogel was immersed in a preweight 30 ml beaker containing water. The wet hydrogel was removed and the beaker weight again. The lost water represented the amount of water that was absorbed by the rice hydrogel. The test was repeated 10 times.

3. Results

Rice hydrogel can be made from Thai rice starch by cross-linking with glutaraldehyde. It has interconnected porous channels throughout the mass. The dry weight is about 2.5 mg/ml. After burning the remaining ash was 0.01%. Every piece of rice hydrogel was absolutely sterile. The rice hydrogel can be completely dissolved in amylase solution in about 20 min. The hydrogel can absorb water about 40 times its dry weight.

Table 1. The results of laboratory test for hemostatic rice hydrogel .

No	Burning (%)	Sterilization	Degradation (min)	Water absorption (times of dry weight)
1	0.01	no growth	19.5	38
2	0.01	no growth	18.5	38
3	0.01	no growth	21.0	42
4	0.01	no growth	18.5	40
5	0.01	no growth	20.5	41
6	0.01	no growth	20.5	43
7	0.01	no growth	21.5	43
8	0.01	no growth	18.0	42
9	0.01	no growth	20.5	39
10	0.01	no growth	22.0	40
mean	0.01	-	20.05	40.6

4. Conclusion

We can make an innovative hemostatic rice hydrogel for the first time in the world in Thailand. This hydrogel is made following pharmaceutical standards for correct manufacturing, packaging, sterilization and basic laboratory tests. It must undergo further research in animal and clinical trials.

5. References

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