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Case Reports of Bedsores Using *Aloe Vera* Gel Powder with High Molecular Weight

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ABSTRACT
It has been reported that the Japanese have higher rate of life expectancy and that Japan is rapidly becoming a super aging society. Almost 5 per cent of the aged, who develop diseases such as cerebrovascular related disorders, mental problems, fractures, cancer and infections also end up suffering from bedsores. It has been found that patients often opt for treatment, when the bedsores become very severe and adding more complications in their treatment. It may be presumed that prevention and early detection are vital for the treatment of bed sores. In our present study, we have tested herbal formulations having Aloe vera gel powder for its efficacy and activity on bed sores. Aloe vera gel powder with high molecular weight (AHM) was prepared from the gel part, by washing with running water using the patented freeze-drying under micro wave and far infra red irradiations in which barbaloin content was less than 10 ppm in powder form. The treatment was given by applying the macromolecule aloe ointment for bedsores from I degree to Π degree ulcer patients. The results have shown that AHM in the ointment form indicated a high possibility to cure bedsores. Being very difficult to cure, due to the patient's peculiar conditions such as old age, inability of the patient to turn by himself/herself and also due to complications caused by other symptoms. We were able to confirm the effectiveness of the macromolecule aloe ointment in four cases of bedsores with two cases of positive control, using the Design Score and by checking the side effects. In this study, our report is based on the preclinical trials for bedsores by the external use of the macromolecule aloe ointment.
***Key words*:** case reports, bedsores, macromolecule *Aloe vera* ointment

INTRODUCTION

The topical application of *Aloe vera* gel is perhaps effective in the treatment of psoriasis (1-2), genital herpes (3-4) and decubitus (5-6). However, there is confusion about Aloe preparations which were applied in clinical studies (7). Chemical and physical evidences are needed for healing effects of Aloe preparations. Utilising the change in mode of preparation method and material as a natural product is required. Recently, upon application of *Aloe vera* gel in genuine form to preclinical studies, we developed a new technology for preparing *Aloe vera* gel powder with high molecular weight. This was done by using a patented hybrid-dry system, which has been applied to make dry substance without tissue and cellular damages in the field of natural sources rich in water content, such as fish, seaweeds and *Aloe vera* gel etc. Topical application of some *Aloe vera* gel preparations causes contact dermatitis in rare cases and *aloin* could be an irritant to the skin (8). The International Aloe Science Council (IASC) has authorized that the content of *aloin* in *Aloe vera* gel preparation is less than 50 ppm. Topical application of *Aloe vera* is not an effective preservative for radiation-induced injuries,

and whether it promotes wound healing is unclear (7). There are few reports on the effectiveness of *Aloe vera* gel therapies on chronic wounds (9). A recent study of *Aloe vera* gel for burn healing concluded that the group that was being given *Aloe vera* recorded a healing time that was 8.79 days shorter than those in the control group (p=0.006) (10). Present case reports of AHM in the ointment preparation were carried out to determine the efficacy of bedsores after preliminary humidity test of the aloe ointment.

MATERIAL AND METHODS

Object

Four patients identified as I degree, Π degree or IΠ degree with ulcers and who had been hospitalized at Taihei Hospital in Japan.

Trial Period

Eight months during September, 2005 and October, 2008.

Consent of Patient

We obtained the consent of the patients for this treatment by document or word of mouth by free will after explaining the contents to them before proceeding with the treatment. All procedures used in the protocol were in accordance with the Helsinki Declaration. In addition, we obtained the consent from the patient's family; when the patient was unable to judge through Hospital Committee equivalent to the Institutional Review Board.

Material

Aloe vera L. plant, syn. *A.barbadensis* Miller, cultivated in Okinawa, Japan, was compared and determined to be *Aloe vera* L. (Herbarium number 54-3 in Medicinal garden, Fukuyama University by Prof A.Yagi). The macromolecule aloe ointment is a mixture of the hydrophilic ointment and AHM at 0.1% by weight. AHM were prepared from the gel part washed with running water by the patented freeze-drying under microwave and far infra red irradiations in which barbaloin content was less than 10 ppm in powder form. AHM MW: 1,119,500 D by HPLC analysis: colony formulation unit, less than 300/g, Na^+ approx. 430 mg/100g, Ca^{2+} approx. 2100 mg/100g, Chemical shifts of AHM on ^1H- and ^{13}C-NMR were determined in D_2O with a JOEL JNM alpha-400 at 400 and 100 MHz for proton and carbon, respectively. The infra red spectra were obtained with a FTIR-8600PC, Shimadzu, Japan.

^1H NMR (ppm, 10 mg/ml in D_2O at 34.3℃: TMS as an internal standard): 2.12 (s, CH_3COO), 2.58 (br. s, -C(OH)-CH_2COOH, citric acid), 2.74, 2.78 (d.-CH_2-CH(OH)COOH, malic acid), 3.4-4.0 polysaccharides, -CH(OH)CH(OH)-),3.97(m,-CH_2CH(OH)COOH,malic acid), 4.18 (m,-CH_2-CH(OH)COOH, malic acid)、 5.19, 5.20 (br. s. anomeric proton of the non-reducing carbon atom), assigned by comparison with ^1H NMR data base of IASC.

^{13}C NMR (ppm, 10 mg/ml in D_2O at 34.3 ℃: TMS as an internal standard): 62.1(C6), 70.9, 75.4, 77.0, 77.1, 97.1 (C1), 175.9 (CH_3COO). IR (KBr) vmax: 3381(OH), 2922 (COOH,-NH-), 1735 (CH_3COO), 1597(-NHCO-), 1245 (-CHOH), 1033(-CHOH). Carbohydrate and protein content in AHM was determined according to phenol-sulphuric acid (11) and Lowry method (12), to 90% and 7%, respectively. A glycoprotein fraction, verectin, composed of carbohydrate and protein in a ratio of 10.7% and 82.0%, respectively with MW of 29KD (13), was contained in a ratio of 20% in AHM by immuno-chemical assay (14). Humidity test of cuticle was carried out by using ASA-M2/SS, ASAHI BIOMED, Yokohama, Japan. The physical conversion in less than 2 hours was applied with the nutritional control side by side.

Pre-treatment: In case the skin ulcer therapeutic drug had been used on a patient, then an isotonic sodium chloride solution was applied for washing it out and a gauze dressing was put for 7 days. As a positive control, gentamicin ointment was applied.

Treatment

After the skin ulcer therapeutic drug had been washed out, AHM ointment was applied to the diseased part once or twice a day after washing it with an isotonic sodium chloride solution.

Prohibited Medicine

Through the trial term, all medications, such as steroids, blood stream accelerants and others which influence efficacy of the aloe ointment were completely avoided.

Observation

According to Design Score, all the diseased part was periodically evaluated every month.

Side Effects

Monthly medical examination through interview and an ocular check up on the side effects was done. In case, side effects were found, the tracing survey was conducted till they disappeared. Simultaneously, the analysis of these side effects on sort, degree, day of appearance, progress, treatment, day of disappearance and causality with the macromolecule aloe ointment was also conducted.

Judgment

The judgment was given for 3 months after starting the treatment.

i) Judgment criterions in Design Score are as follows:

Score	Criteria
Extremely improved	improved 6 points and more
Improved	Improved 3 points and more
Slightly improved	Improved less than 3 points
Not Improved	Improved 0 point
Aggravation	Minus points

ii) Design Score (A table is prepared to judge a process and condition by points)

D → Depth point 0 – 5 ;

E → Exudates point 0 - 3

Size point 0 - 6

I → Inflammation / Infection point 0 – 3 ;

G → Granulation tissue point 0 – 5 ;

N → Necrotic tissue point 0 – 2 ;

P → Pocket point 0 - 4 ;

The ulcer square

It was done by measuring the dimension covering longer diameter (cm) × shorter diameter (cm). In each item, point 0 indicated cured or unrecognized, and if the point is more which indicated the condition has worsened.

For e.g. Case 1: (1.2.3.2.1.0.1.) = (D=1. E=2. S=3. I=2. G=1. N=0. P=1) = point 10

Case 2: (1.1.1.0.0.0.0.) = point 3: Seven points were reduced.

At the time of Case 2, the diseased part was Extremely Improved than at the time of Case 1. The judgment was done according to 1) above. The treatment was recorded at the beginning using the Design Score. Thereafter, every check was recorded, and compared with that of the starting treatment, and judged.

Availability judgment of the macromolecule aloe ointment:

The availability was judged according to the reduced points in Design Score and the occurrence (or none) of side effects.

CASE STUDY

CASE 1 age 52, female

First medical examination: December 7, 2002.

History: cerebral infantile paralysis, cervix myelopathy, symptom-related epilepsy, a sacral region bedsore.

Present illness: The patient was bedridden since childhood. A bedsore occurred on her sacral region, it improved and later reoccurred. A surgical operation of the bedsore was performed at another hospital in 2001. She was hospitalized for medical treatment in 2002. At this time, a skin ulcer of 3 cm diameter was found in her sacral region. A simple cellular growth was observed in the affected part, and it was surgically removed in June of 2003. Later, the ulcer enlarged to 10 cms. With regular washing and external treatment, the affected part subsided gradually. In November 2005, The Design Score of the affected part was point 4 (1.1.1.1.0.0.0.). At this stage, honey was externally applied on the affected part. .

Process: After conducting the washing out process for 7 days, the treatment was started on December 7, 2005.by applying macromolecule aloe ointment after washing the diseased part with an isotonic sodium chloride solution.

THE DESIGN SCORE at the start was point 4.

THE DESIGN SCORE on December 15, 2005 was point 0 and the epidermis was formed. No side effect was found.

Result: IMPROVED (no side effect observed)

CASE 2 age 80, female.

First medical examination: May 4, 2002.

History: abolished business-related syndrome, pulmonary emphysema, frequent occurrence related-cerebral infraction.

Present illness: She was hospitalized for pneumonia at the age of 77. At 78, she suffered a fracture and has been bedridden since then. After that she suffered from a syndrome for ash and a sacral region bedsore. On September 28, 2005, DESIGN SCORE on her affected part was point 5 (2.1.1.0.1.0.0.). At this stage, honey was externally applied on her affected part.

Process: Same treatment as CASE 1. It was started on November 30, 2005. DESIGN SCORE at the start was point 5.

DESIGN SCORE on January 18, 2006 (6 weeks) was point 0 and the epidermis was formed.

Result IMPROVED (no side effects observed)

CASE 3: age 92, male.

First medical examination: November 24, 2005

History: senile dementia, symptomatic epilepsy, bedsore on heels.

Present illness: The patient had dementia and became bedridden at the age of 88.

Since he was hospitalized, he developed a skin ulcer on his right heel which was 2 cm in diameter. He also developed an ulcer sized 3 cm with necrotic tissue on his left heel. On November 24, 2005, DESIGN SCORE was 11 points (3.2.2.1.2.1.0.).

Process: Same treatment as applied in CASE 1 and CASE 2. It was started on December 1, 2005. The affected portion of the right heel was epithelised on January 11, 2006 (45 days). On the same day, it was observed that DESIGN SCORE of the left heel had become 2 points (1.0.1.0.0.0.0.).

Result: EXTREMELY IMPROVED (no side effects observed).

CASE 4 age 87, female.

First medical examination: October 12, 2000.

History: chronic kidney failure, diabetes, atrium fibrillation, frequent occurrence related-cerebral infarction, cerebrum senile dementia.

Present illness: The patient suffered from cerebral infarction at the age of 79 and gradually became bedridden. She was hospitalized in 2000. She had a renal insufficiency aggravation in early January, 2006. At that time she had a skin ulcer in her trochanter part, sized 2.5 cm diameter. The DESIGN SCORE was 16 points (3.2.2.3.5.1.0.). Surgery was done to remove it. By February 8, 2006 the DESIGN SCORE had improved to 9 points (3.2.1.0.2.1.0.).

Process: Same treatment as other cases was applied and was started on February 8, 2006. In one month the DESIGN SCORE improved to 4 points (1.1.1.0.1.0.0.). The affected portion was epithelised on April 1, 2006, which means the DESIGN SCORE became 0 point.

Result: EXTREMLY IMPROVED (no side effects observed).

CASE 5: A positive control study, age: 63, female

First medical examination: May 12, 2005

History: Parkinson's disease

Present Illness: The patient suffered from Parkinson's disease when she was around 50 years old. The disease gradually worsened and she could not walk by herself. Finally she was hospitalized for medical treatment in 2005. At the time of hospitalization, a skin ulcer of diameter 5 cm was seen on her left hip.

Process: From August 29, 2008, external application of gentamicin ointment was started. At this stage the DESIGN SCORE of her affected part was point 9 (2.2.2.0.2.0.1). After one month of treatment, the DESIGN SCORE did not change without any side effect.

Result: Not improved (No side effect observed)

CASE 6: A positive control study age: 90 male

First medical examination: October 17, 2006

History: cerebral infarction and diabetes

Present illness: The patient could not walk by himself and was hospitalized. He suffered from paralysis on his right side and had become bedridden since then. At the time of hospitalization a skin ulcer of diameter 5 cm was found in the sacral region.

Process: From August 29, 2008, external application of gentamicin ointment was started. At this stage the DESIGN SCORE of the affected part was point 6 (2.2.1.0.1.0.0). After two weeks of treatment, the DESIGN SCORE was point 7 (2.2.2.0.1.0.0) and after one month of treatment, the DESIGN SCORE was point 8 (3.2.2.0.1.0.0) without any side effects.

Result: AGGRAVATED

RESULTS

Humidity test

Average value of humidity (admittance, micro S, n=6) at each measurement point of stratum corneum epidermidis (cuticle) on arm after 15, 60 and 90 min are shown in Table 1. Also, as shown in Table 1, the

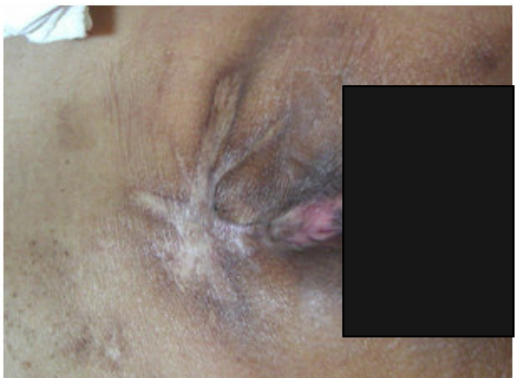
Table 1: Humidity test of Aloe powder with high molecular weight produced by hybrid- dry system to patients (n=15) by the ointment preparation (1.6 mg/ml).

Age, sex	15 m	60 m	90 m
21 F	12.62	16.28	15.23
23 F	6.60	9.95	7.62
24 F1	5.88	5.27	6.58
24 F2	4.65	5.45	5.10
28 F	9.30	32.02	34.77
37 F	21.33	23.58	24.07
38 F	22.05	43.48	28.83
39 F	10.15	34.82	43.22
40 F	10.98	12.95	14.17
43 M	15.83	29.85	25.15
43 F	9.32	30.40	19.38
44 F	10.98	12.95	14.17
46 F1	12.89	22.23	63.18
46 F2	16.47	43.48	28.83
48 F	10.86	31.78	19.00

Table 2: Design Score

Case no.	Age and gender	Design score			Side effects	Result
		Start	1st Month	2nd Month		
1	52, female	4	0		none	Improved
2	80, female	5	2		none	Improved
3	92, male	11	2		none	Extremely improved
4	87, female	9	4	0	none	Extremely improved
5	63, female	9			none	Not improved
6	90, male	6	8		none	Aggravated

Figure 1: Case 1 ; before treatment



Case 1 ; After treatment

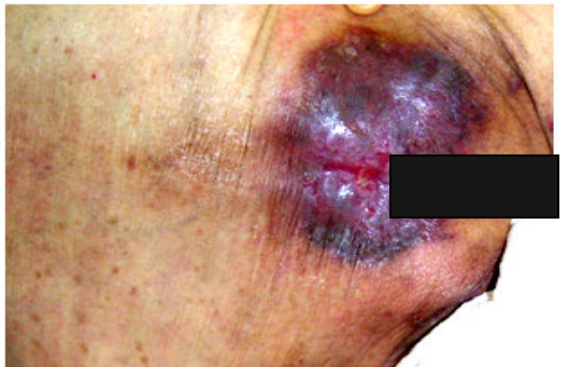
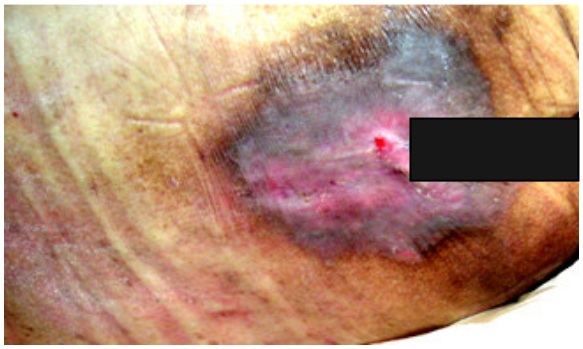


Figure 2: Case 2 ; before treatment



Case 2 ; After treatment

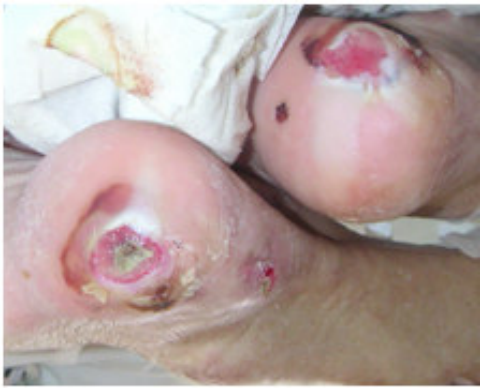
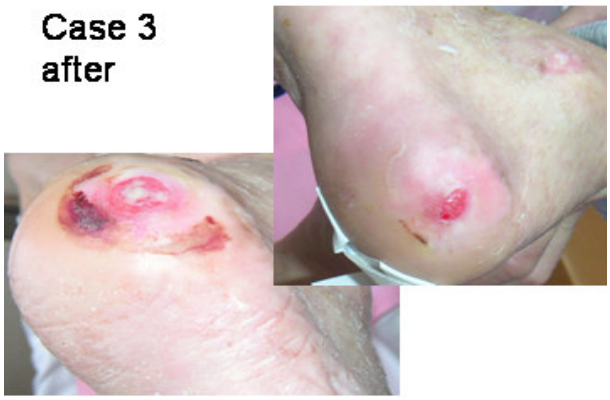


Figure 3: Case 3 ; before treatment



Case 3; After treatment

aloe ointment exhibited a tendency to conserve humidity on cuticle during 90 min at least.

In the preliminary test, the patient responders, concentration of dose and test time to the powder solution after patch test and informed consent were determined. Negative reaction of the patients to patch test was obtained. Case reports of four patients comparing with that of two positive controls, showed improvement by use of aloe ointment in DESIGN SCORE without any side effects.

DISCUSSION

In an earlier *in-vitro* experiment, verectin, a glycoprotein fraction isolated from *Aloe vera* gel, showed a proliferation-promoting activity on human dermal (NB1RGB) and hamster cells (13). Verectin also inhibited the generation of O_2- by xanthine-xanthine oxidase and cyclooxygenase (Cox)-2 and thromboxane (Tx) A_2 synthase. Inhibition of Cox-2 and Tx A_2 synthase level is closely linked to prostaglandins levels in tissue injury, and verectin fraction plays an important role in the anti-inflammatory activity of *Aloe vera* leaf gel (15). Furthermore, ELISA using polyclonal rabbit anti-verectin anti-serum indicated the localization and identification of verectin in *Aloe vera* leaf gel and commercial *Aloe vera* gel products (14),Verectin content in AHM was shown at 20% concentration.

As a preliminary study, we performed humidity test of the aloe ointment to patient responders. Table 1 shows possible conservation of humidity on cuticle by AHM in the ointment preparation. AHM having acetyl groups in macromolecular mannan (16 and 17) may be easily dispersed to form the hydrophilic ointment as 0.1% by weight and used as the material for this bedsore clinical trials. The ointment contains macromolecular polysaccharides and glycoprotein as the crucial ingredients of fresh *Aloe vera* gel. The results of this trial showed that AHM in the ointment preparation has a high possibility to cure bedsores. It has often been stated that bedsores are one of the most difficult problems to cure because of the patient's peculiar conditions such as old age, inability to turn by himself / herself and complications caused by other symptoms. The success of aloe vera gel in the treatment of bedsores may be attributed to its wound-healing and anti-inflammatory activities, with no side effects, has high competence of epithelialisation followed by tissue and texture restoration. Further, it has potential for quick remedy, which will greatly help the aged patient's QOL – Quality of Life and have high efficacy compared to gentamicin ointment.

The results showed that AHM contains rich and good macromolecular polysaccharides with acetyl groups and glycoprotein fraction, verectin, to cure bedsores. The combined action of these ingredients which showed anti-oxidation and prostaglandin 2-inhibition *in vitro* may be effective in curing bedsores. AHM ointment was shown to penetrate tissue, relieve pain, reduce inflammation and increase blood supply to the damaged area. Our hypothesis is that macromolecular polysaccharides as an adjuvant, can physically absorb and hold the exudates through the osmotic pressure differences, so that the desirable moisture condition to cure wounds is maintained. It also provides a rich nutrition, playing a part in the regeneration of tissue, texture and epidermis that need to be restored. In addition glycoprotein fraction such as verectin has attributed for its anti-inflammatory activity and wound-healing property (18 & 19). The remarkable point of AHM preserved by new technology is that it do

not lose the high molecular structure with acetyl groups and glycoprotein, and verectin moiety for the first time. Therapeutic trials not only for bedsores but for general wound-healing using AHM ointment are fully expected.

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