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Original article

Innovation of Colostomy Appliance from Deproteinised Natural Rubber (DPNR)

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Abstract

Background and Objectives: In Thailand, the Colorectal cancer incidence rate is 127.7 per 100,000 for men and 125.5 per 100,000 for women. Twenty percent of these patients have a permanent or temporary colostomy that needs colostomy flange. The colostomy flanges that are available in Thailand are imported and are expensive. Thailand is an agricultural country and is the leading natural rubber producer and exporter. Flange made within the country would cost significantly less than the imported ones. Nevertheless, the safety standard is the main point that we considered. ***Material and methods:*** This study is an experimental prospective non-randomized control trial study at Songklanagarind Hospital. The study was approved and monitored by the ethical committee of Songklanagarind Hospital. Thailand Institute of Scientific and Technological Research (TISTR) approved the animal phase. Then, the volunteer phase was performed to conduct the best one of the material formulas for colostomy flange. ***Result:*** Fresh latex has 16.66% dermatitis and no anaphylaxis. Block latex and concentrated latex has the same allergic symptoms (13.1% dermatitis) but Block latex show a lower rate of other symptoms including itch and hyperpigmentation. Block latex was selected to produce Deproteinised Natural Rubber (DPNR). Three Deproteinised Natural Rubbers (DPNR) were achieved. Rubber formula 2 causes the lowest allergic symptoms; there is no anaphylaxis and only 0.5% dermatitis. ***Conclusion:*** Rubber formula 2 is the lowest prevalence of latex allergy in this study and is a lower prevalence compared to the previous study. It is suggested that Rubber formula 2 is safe to be the material for producing a colostomy flange. However, clinical trial and data must be collected during the patient phase trail.

Keywords: ***colostomy flange, natural rubber, colostomy equipment.***

Introduction

In Thailand, the Colorectal cancer incidence rate is 127.7 per 100,000 for men and 125.5 per 100,000 for women.1 Twenty percent of these patients have a permanent or temporary colostomy that needs colostomy equipment. Colostomy flange is one of the materials available. The colostomy flanges that are available in Thailand are imported and are expensive. Data from Songklanagarind Hospital show that the expenses rise higher each year. Twenty-four thousand to twenty-six thousand pieces which are ordered per year cost nearly 3.5 million baht.

The study of latex allergy for both all patients and medical fatality (staff) had been done from 1987 to 1997. Prevalence of latex allergy in occupationally exposed groups and general population groups vary in 1-12%2-6 and 0-18%[4,7-11] respectively. After this period, there have had no further information, which could be possible that it was just an early age of latex products.

The major issues of latex allergy lead to the question whether the latex products are safe enough to utilize for hypersensitive groups. Latex allergy could be shown as Type I Hypersensitivity (Anaphylaxis) and Type IV Hypersensitivity (Allergic contact dermatitis) which can be diagnosed using medical history, signs, and symptoms.

The protein content of latex averages about 1% but varies depending on several factors including genetic factors, chemical factors, and the metabolic makeup of the rubber tree. Many of the

proteins from natural rubber latex have been implicated in the pathogenesis and sensitization resulting in allergy and immediate hypersensitivity responses.[12] To date, 11 NRL proteins have been characterized and designated as allergens, Hev b 1 to Hev b 11.[13]

Table 1: Natural rubber latex proteins

Name	Molecular mass (kDa)
Hev b 1	14.6
Hev b 2	34-36
Hev b 3	24-27
Hev b 4	110/50
Hev b 5	16-24
Hev b 6	20/4.7
Hev b 7	43-36
Hev b 8	14-14.2
Hev b 9	51
Hev b 10	22-26
Hev b 11	33

Thailand is an agricultural country and is the leading natural rubber producer and exporter. Flange made within the country would cost significantly less than the imported ones which would make the equipment affordable for both the Thai government and the patients. Nevertheless, the safety standard is the main point that we considered. So the material that is provided to produce colostomy flange must have the lowest allergic reaction profile.

Purpose

To get the natural latex material with lowest allergic reaction profile.

Methods

There are 2 phases performed in this study.

The 1st phase: animal phase

Acute dermal irritation Test in Rabbits was performed by the Thailand Institute of Scientific and Technological Research (TISTR).[14]

The test of Acute Dermal Irritation / Corrosion was conducted according to the Test Guideline (TG) No.404 of the OECD Guidelines for testing of chemicals (2002).

Three rabbits were employed and acclimatized to the laboratory environment for one week. One day before experimentation, an area of skin approximately 10 cm x 10 cm on the dorso-lumbar region of each rabbit was clipped free of hairs. Two areas of shaven skin approximately 2.5 cm x 2.5 cm were selected. The weight 0.5g of "Rubber sheet 1" was moistened with distilled water and then introduced on to a 2.5 cm x 2.5 cm gauze patch, which was served as a treated patch while 0.5 ml of distilled water on another patch was served as a control patch. Both patches were applied to the selected skin sites on each rabbit. The patches were then secured to the skin by transpore adhesive tape. The entire trunk of the rabbit was wrapped with elastic cloth to avoid dislocation of the patches for 4 hrs. At the end of the exposure period, all patches were removed and gently wiped the treated skin with moistened cotton wool to remove any residual test material. The animals were assessed for the degree of erythema and edema evidence on each site at 1, 24, 48 and 72 hours after removal of the patches. Further observation would be needed, as necessary, to establish the reversibility if the irritation sign(s) still existed, but would not exceed 14 days after application. In addition to the observation of irritation, any lesion and other toxic effects were recorded. The skin reactions were independently scored by two inspectors using the numerical scoring system as follows.

Erythema and eschar formation:	**score**
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation	4
Edema formation	**score**
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond the area of exposure)	4

Reversibility of dermal lesions should be considered in evaluating irritant responses. When responses such as alopecia (limited area), hyperkeratosis, hyperplasia, and scaling, persist to the end of the 14-day observation period, the test chemical should be considered an irritant.[14]

The 2nd phase: Volunteers phase

This study is an experimental prospective non-randomized control trial study at Songklanagarind Hospital. The study was approved and monitored by the ethical committee of Songklanagarind Hospital.

Phase 2.1: Compare Rubber sheet from fresh latex, concentrated latex and block rubber

We included 200 volunteers (100 men and 100 women) without latex allergic history. The study was conducted in May 2014. Allergic reaction profiles were examined. All volunteers were applied with three Rubber sheets from fresh latex, concentrated latex and block rubber on their abdomen for 1 week. Allergic symptoms were observed after one week. If any volunteers feel uncomfortable before one week, they are allowed to early come back to the clinic for evaluating the condition, gathering all the data, and analyzing whether such volunteers should stop the study. After 1 week, all volunteers came back and were examined to the allergic response by 2 clinicians. Allergic contact dermatitis was diagnosed in volunteers who had one of these clinical signs; Erythema, vesiculation, lichenification, fissuring.[15] Anaphylaxis was diagnosed by the World Allergy Organization Clinical Criteria for Diagnosing Anaphylaxis.[16]

Phase 2.2: Compare three material formulas of colostomy flange

After we picked up the best rubber sheet from study phase 2.1, three material formulas were prepared using different methods. The three material formulas of colostomy flange are Deproteinised Natural Rubber (DPNR). We included 200 volunteers (100 men and 100 women) without latex allergic history. The study was conducted in June 2014. Allergic reaction profiles were examined. There are 200 volunteers (100 men and 100 women) in this phase of the study. All volunteers were applied with three material formulas of colostomy flange on their abdomen for 1 week. Allergic symptoms were observed after one week. If any volunteers feel uncomfortable before one week, they are allowed to early come back to the clinic for evaluating the condition, gathering all the data, and analyzing whether such volunteers should stop the study. After 1 week, all volunteers came back and were examined to the allergic response by 2 clinicians. Allergic contact dermatitis

and anaphylaxis were diagnosed using the same criteria in *Phase 2.1*.

Additional laboratory study called Dot Blot method to detect Rubber elongation factor (REF)[17] in Hev b1 protein which is the latex allergic protein was performed using 3 rubber sheets from phase 2.1 and 3 material formulas of colostomy flange from *Phase 2.2*.

Result

The 1st phase; animal phase

After removal of the patches, the treated skin of each rabbit was observed for skin reactions at the 1st, 24th, 48th, and 72nd hrs. The results showed that all three treated rabbits exhibited slight erythema of skin observed at the 1st hour. The recovery of this skin reaction occurred within 48 and 72 hrs of the observation period, respectively.

The 2nd phase: Volunteers phase

Phase 2.1

198 volunteers were finished at the 1st week of the study. Median age is 20 years old. Two patients were excluded from the study due to loss follow up.

Table 2: Baseline characteristic of Phase 2.1 volunteers

Characteristics	Volunteers (N=198)
Median Age year (IQR)	20(20,21)
Gender	
Male	98
Female	100
Underlying disease	
Allergic Rhinitis	24
G6PD	3
Asthma	1
No	170
Food Allergy	
Yes	12
No	186
Drug Allergy	
Yes	11
No	187
Chemical Allergy	
Yes	24
No	173

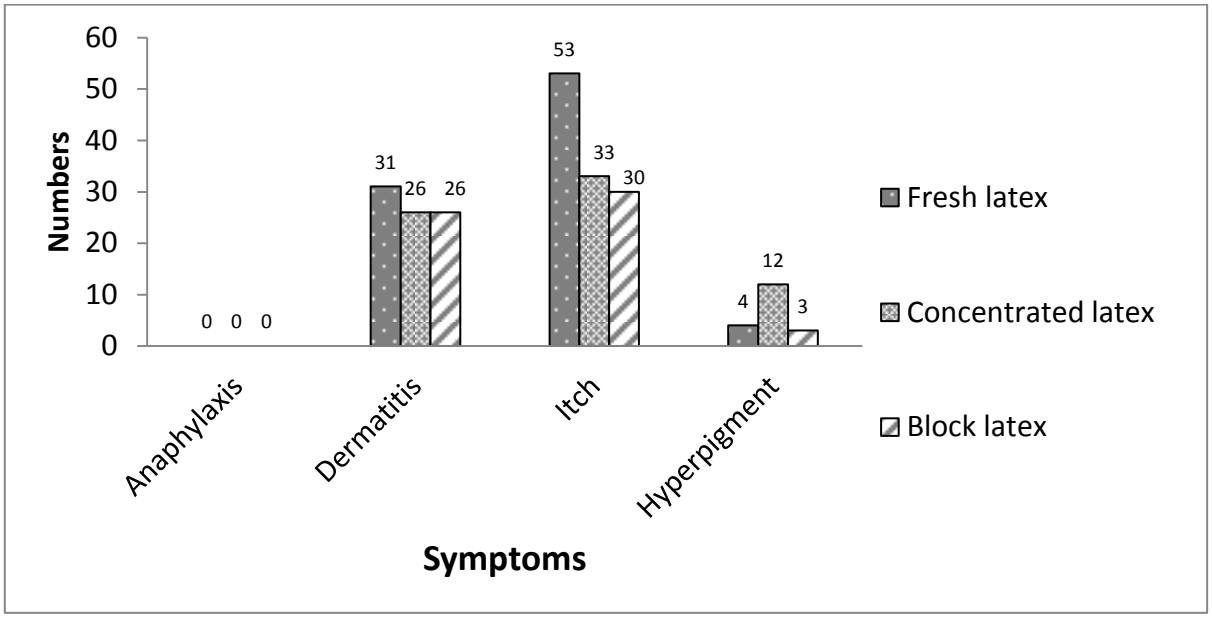

Figure 1: A numbers of volunteers who showed allergic symptoms from each type of latex

The results show that Block latex and concentrated latex has the same allergic symptoms (13.1% dermatitis) but Block latex show a lower rate of other symptoms including itch and hyperpigmentation. Fresh latex has 16.66% dermatitis and no anaphylaxis.

The median onset of dermatitis of fresh latex, concentrated latex, and block latex was 72, 48 and 48 hours respectively. The median duration of recovery for all formulas was 48, 24, and 24 hours respectively.

Phase 2.2

All 200 volunteers had completed the study. The mean age of these volunteers was 21 years old.

Table 3: Baseline characteristic of Phase 2.2 volunteers

Characteristics	Volunteers (N=200)
Median Age year (SD)	21.8±4
Gender	
Male	100
Female	100
Underlying disease	
Allergic Rhinitis	14
G6PD	1
Asthma	0
Other	5
No	180
Food Allergy	
Yes	8
No	192
Drug Allergy	
Yes	12
No	188
Chemical Allergy	
Yes	2
No	198

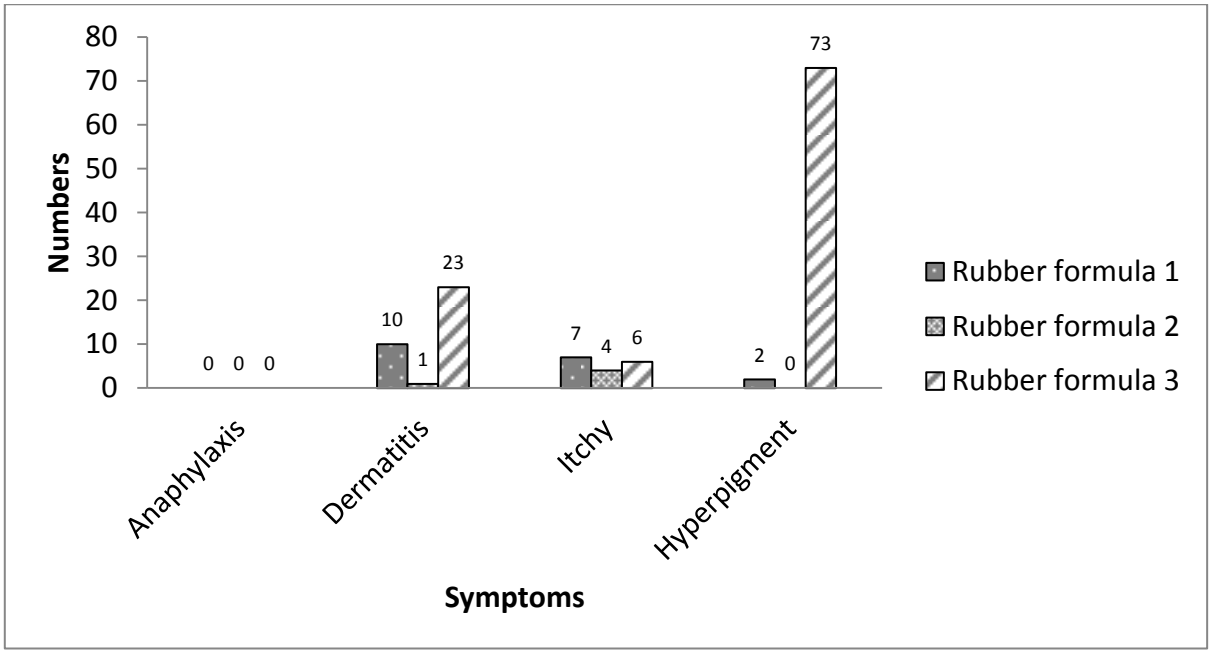

Figure 2: A numbers of volunteers who showed allergic symptoms with each rubber formula

The result shows that Rubber formula 2 has the lowest allergic symptoms; there is no anaphylaxis and only 0.5% dermatitis.

The median onset of dermatitis of rubber formula 1, 2 and 3 was 96, 60 and 168 hours respectively. The median duration of recovery for all formulas was 24 hours.

Rubber elongation factor (REF) in Hev b1 protein was detected by Dot Blot method as Figure 3.

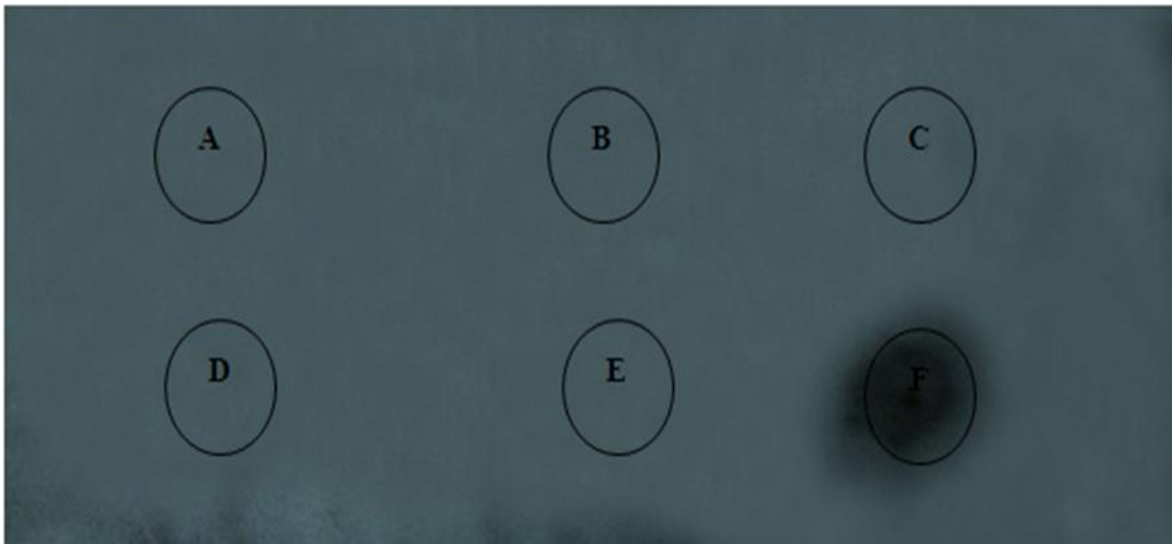

Figure 3: Dot Blot method result detecting Rubber elongation factor (REF) in Hev b1 protein (A; Rubber formula 1, B; Rubber formula 2, C; Rubber formula 3, D; Block latex, E; Concentrated latex, F; Fresh latex.)

Discussion

There is no anaphylaxis allergy to all three types of latex. Prevalence of latex allergy in this study is 13%-16% which slightly higher than the previous studies that included the general populations in their studies. Among three latexes, Block latex is the best one to produce material formulas of colostomy flange. Fresh latex shows the highest prevalence of latex allergy (16.66%) compatible with the Laboratory test (Rubber elongation factor).

There is no anaphylaxis allergy to all three material formulas of colostomy flange in phase 2.2. Rubber formula 2 shows the lowest dermatitis (0.5%) compared with the three materials in this study. Also, Rubber formula 2 shows a lower prevalence of latex allergy compared with the previous study.

Conclusion

Rubber formula 2 is the lowest prevalence of latex allergy in this study and a lower prevalence compared with the previous study. It is suggested that Rubber formula 2 is safe to be the material for producing a colostomy flange. However, clinical trial and data must be collected during the patient phase trial.

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