International Surgery Journal
Vasuki V et al. Int Surg J. 2017 Apr;4(4):1209-1216
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20171020

Original Research Article

Comparative study of papaya dressing versus normal saline dressing in healing of ulcers

Vasuki V., Thanmaran N. B., Vimalakaran B., Madan K.*

Department of General Surgery, Kilpauk Medical College and Hospital, Chennai, Tamilnadu, India

Received: 21 February 2017
Accepted: 07 March 2017

***Correspondence:**
Dr. Madan K.,
E-mail: dr.madankuppusamy23@gmail.com

ABSTRACT

Background: Chronic non-healing wounds pose a remarkable challenge to health professionals and drain our resources. In recent years, prevalence of diabetic foot ulcers is growing at epidemic proportion in India and worldwide. There are various modalities available for wound debridement. In present study, authors have compared two debridement methods, one which we use regularly in their hospital, wet to dry normal saline dressing and enzymatic debridement with papaya.
Methods: This was a randomized, comparative interventional study of 100 patients carried out in Kilpauk Medical College Hospital from August 2013 to August 2014 to compare to efficacy of papaya dressing over normal saline dressing in chronic non-healing wounds.
Results: The mean reduction in slough/necrotic tissue in at time of inclusion in study and four week after the study was assessed. In saline dressing, mean reduction was 13.156, standard deviation 3.4558. The mean reduction in slough/necrotic tissue in papaya dressing 10.5, standard deviation 0.7071. There was significant difference in percentage reduction in slough/necrotic tissue within the two groups. Similarly, for the cases with active ulcer, the size assessment at the time of inclusion in the study and three week after was again analysed using student t-test and the mean ulcer size in papaya dressing 2.5062 and standard deviation 1.504. Mean ulcer size in normal saline dressing 2.1564 and standard deviation 1.2961.
Conclusions: Present study concluded that favourable and significant ulcer healing rate with improvement and reduction in clinical severity suggests that enzymatic debridement with papaya dressing plays an important role in management of chronic non-healing ulcers.

Keywords: Non-healing ulcer, Normal saline dressing, Papaya dressing

INTRODUCTION

Wound management has been a fundamental part of general surgical practice since ancient times. Chronic non-healing wounds pose a remarkable challenge to health professionals and drain our resources. In recent years, prevalence of diabetic foot ulcers is growing at epidemic proportion in India and worldwide and they have become the major contributors of chronic non-healing wounds.

Although wound management is a day-to-day activity in surgical wards, there is always scope for betterment of our surgical practice. Therapeutic strategies have been evolving over the years and there are varieties of dressing options available for wound bed preparation, wound cover, activation of wound healing and repair. Technological advancements have also resulted in topical applications of recombinant platelet derived growth factors and bio engineered skin substitutes for skin coverage in wound management.

The sequence of wound repair is controlled in each stage by activators and inhibitors that are naturally produced by our immune system. Cellular migration, proliferation, matrix deposition and remodelling which causes progress in wound healing.[1] Devitalized tissue and exudates act as mechanical barrier to migration of cells and provides an environment ideal for bacterial proliferation.[2] Due to the presence of devitalized tissue there is excess production of pro-inflammatory cytokines and prolongation of inflammatory response.[3]

Thus, wound bed preparation plays a crucial role in achieving a conducive environment for wound healing. There are various modalities available for wound debridement; most of these methods are covered in this review with major emphasis on enzymatic wound debridement with papaya. In present study, authors have compared two debridement methods, one which we use regularly in their hospital, wet to dry normal saline dressing and enzymatic debridement with papaya.

Aim

To compare the effectiveness of papaya versus normal saline debridement in healing of ulcers.

METHODS

This was a randomized, comparative interventional study carried out in Kilpauk Medical College Hospital from August 2013 to August 2014. The study was approved by the Institutional ethical committee. The study group comprised of hundred patients with ulcers due to diabetes mellitus, wound infections and post-operative wound dehiscence.

Patients were selected, randomized and divided into two groups.

- Group-1: 50 patients treated with papaya dressing.
- Group-2: 50 patients treated with wet to dry normal saline dressing.

Method of data collection

- Clinical assessment done during time of inclusion.
- Complete history and detailed examination done at inclusion.
- Ulcer and devitalized tissue accurately assessed.
- Measurement of ulcer using sterile gauze and graph paper.
- Area of ulcer calculated in Sq.cm.

Inclusion criteria

- Patients aged more than 20 years with diabetic ulcers and infected ulcers.
- Wagners ulcer grade-II and grade-III.
- Post-operative wound dehiscence.

Wagners ulcer grade

- Grade-I: Superficial ulcers
- Grade-II: Deep ulcers upto subcutaneous tissue exposing soft tissue or bone
- Grade-III: Abscess formation underneath / osteomyelitis.
- Grade-IV: Gangrene of part of tissue / limb / foot.

Exclusion criteria

- Ulcers with severe active infections
- Wagners ulcer grade more than III
- X-Ray features of underlying osteomyelitis
- Diabetic foot with major vascular disease
- Uncontrolled diabetes mellitus
- Patients with hepatic, renal and hematological diseases which impair wound healing
- Patients on immunosuppressive drugs, long term steroid therapy, radio therapy or chemotherapy.

Methods

Study was initially started in 128 patients, 64 patients in each group after randomization.

- 16 patients lost follow up after treatment phase.
- 3 patients died during the follow up phase (2 patients died of CVA and 1 patient died of MI).
- 5 patients went against medical advice during treatment phase.
- There were remaining 104 patients, 53 patients in papaya group and 51 patients in normal saline group. First 50 patients in each group in the random table were taken into the study for comparison.

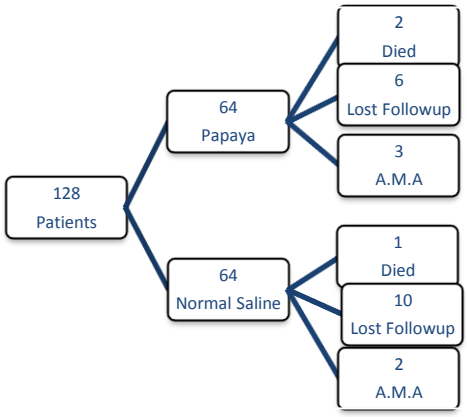

Figure 1: flow chart showing patients receiving normal saline dressing and papaya dressing.

Statistical methods.

- Probability value (P-value) <0.05 the null hypothesis was rejected i.e. P-value <0.05 means there is significant relationship between the two tests.

- Student's t-test (t-test) was used to find the difference between means of the two groups.
- Chi square (χ^2) test was used to find difference between percentages or proportions of categorical outcomes of the two groups.
- Other non-parametric test used to find the significance was Fisher's exact test.

Figure 2: Wound healing with papaya.

Figure 3: Wound contraction with papaya.

Figure 4: Slough reduction with debridement.

RESULTS

58% of the patients were diabetic in the study group. 35% were non-diabetic. 7% had post-operative wound dehiscence. All of them were non-diabetic (Figure 5). Mean age in papaya group was 57.6±9.4502 years. Mean age in normal saline group was 54.2±8.4201 years. There was no significant difference between the two groups (Table 1).

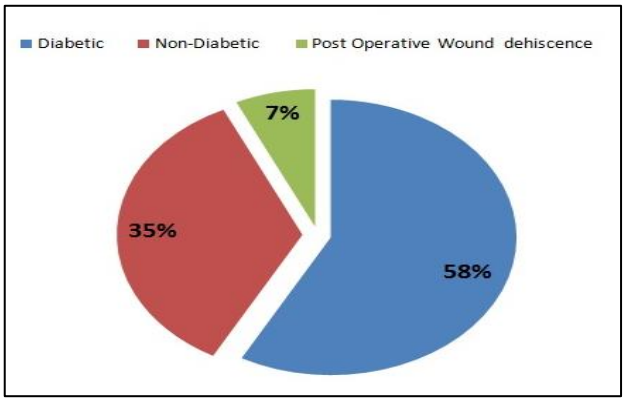

Figure 5: Distribution of patients with diabetic, non-diabetic and post-operative wounds.

Table 1: Mean age distribution in the study.

Group	N	Mean	Std. Dev.	Minimum	Maximum	t-value	p-value
Papaya	50	57.6	9.4502	34	80		
Normal saline	50	54.2	8.4201	37	71	-1.9	0.0604
Total		**55.9**	**8.93515**	**36**	**76**		

Table 2: Sex distribution in the study.

Sex	Dressing			Chi-square value	P-value
	Normal saline	Papaya	Total		
Male	28	27	55	0.0404	0.8407
	56%	54%			
Female	22	23	45		
	44%	46%			
Total	**50**	**50**	**100**		

Table 3: Diabetes distribution in the study.

Diabetes status	Dressing			Chi-square value	P-value
	Normal saline	Papaya	Total		
Yes	28	30	58	0.1642	0.6853
	56%	60%			
No	22	20	42		
	44%	40%			
Total	**50**	**50**	**100**		

Table 4: Distribution of site of ulcer in the study.

Site of ulcer	Dressing		
	Normal saline	Papaya	Total
Abdomen	4	1	5
	8%	2%	
Left ankle	0	1	1
	0%	2%	
Left arm	1	1	2
	2%	2%	
Left foot	16	14	30
	32%	28%	
Left gluteus	0	1	1
	0%	2%	
Left leg	2	3	5
	4%	6%	
Left thigh	0	2	2
	0%	4%	
Right ankle	2	3	5
	4%	6%	
Right arm	1	0	1
	2%	0%	
Right elbow	1	1	2
	2%	2%	
Right foot	14	15	29
	28%	30%	
Right gluteus	0	1	1
	0%	2%	
Right hip	1	2	3
	2%	4%	
Right leg	5	3	8
	10%	6%	
Right thigh	2	0	2
	4%	0%	
Right upper back	0	1	1
	0%	2%	
Scrotum	1	1	2
	2%	2%	
Total	**50**	**50**	**100**

Table 5: Culture and sensitivity pattern in the study.

C/s	Dressing		
	Normal saline	Papaya	Total
E. coli	6	8	14
	12%	16%	
Klebsiella	5	6	11
	10%	12%	
S. aureus	5	4	9
	10%	8%	
Proteus	4	4	8
	8%	8%	
Pseudomonas	2	3	5
	4%	6%	
No growth	28	25	53
	66%	50%	
Total	**50**	**50**	**100**

In papaya group: 54% males and 46% females. In normal saline group: 56% males and 44% females. No significant difference between groups with respect to gender noted (Table 2).

The study has 58 diabetes patients and 42 non-diabetes patients. In papaya group: 60% diabetic patients and 40% non-diabetes patients. In normal saline group: 56% diabetes patients and 44% non-diabetes patients. No significant difference between groups with respect to diabetes patients noted.

Table 4 shows the study has 30% have ulcer in right foot and 29% have ulcer in left foot. Totally 59% have ulcer in lower limbs. Other 41% have ulcer in other areas like thighs, back, arms, scrotum and abdomen.

Culture and sensitivity patterns in both groups were similar. Most frequently grown organism was E. coli followed by Klebsiella (Table 5).

Mean ulcer sizes in both groups were similar. Both groups showed reduction in ulcer size over the 4 weeks period (Table 6).

There was significant difference in percentage reduction in slough/necrotic tissue within the two groups (Table 7).

Table 6: Distribution of mean ulcer size in the study.

Group	Time point	N	Mean	Std.	Minimum	Maximum	t-value	P-value
Papaya	Week 1	34	0.8929	0.4081	0.32	2.11	12.76	<0.0001
	Week 2	49	1.63	0.9775	0.32	4.37	11.67	<0.0001
	Week 3	50	2.5062	1.504	0.5	7.32	11.78	<0.0001
	Week 4	50	3.6966	2.1057	0.86	10.12	12.41	<0.0001
Normal saline	Week 1	31	0.9087	0.4735	0.32	2.08	10.69	<0.0001
	Week 2	49	1.4339	0.9097	0.33	4.33	11.03	<0.0001
	Week 3	50	2.1564	1.2961	0.52	6.24	11.76	<0.0001
	Week 4	50	3.0306	1.7232	0.89	8.47	12.44	<0.0001

Table 7: Slough/necrotic tissue reduction within the study.

Group	Time point	N	Mean	Std	Minimum	Maximum	Difference from baseline	p-value
Normal saline	Baseline	50	62.64	9.5335	40	78		
	Week 1	50	45.88	8.2329	21	62	-16.76	<0.0001
	Week 2	50	32.46	6.792	12	54	-30.18	<0.0001
	Week 3	49	19.9388	5.297	10	32	-43.1633	<0.0001
	Week 4	32	13.1563	3.4558	8	20	-51.1875	<0.0001
Papaya	Baseline	50	64.02	11.6488	32	84		
	Week 1	50	42.26	9.6549	21	68	-21.76	<0.0001
	Week 2	50	25.68	9.0225	8	43	-38.34	<0.0001
	Week 3	33	15.5455	4.8676	10	34	-51.2727	<0.0001
	Week 4	2	10.5	0.7071	10	11	-61	0.0482

Table 8: Slough/necrotic tissue reduction between the study groups.

	Normal saline		Papaya			
Time point	**N**	**Mean**	**N**	**Mean**	**Difference**	**p-value**
Baseline	50	62.64	50	64.02	-1.38	0.5183
Week 1	50	45.88	50	42.26	3.62	0.0464
Week 2	50	32.46	50	25.68	6.78	0.0494
Week 3	49	19.9388	33	15.5455	4.3933	0.0003
Week 4	32	13.1563	2	10.5	2.6563	0.0082

Table 9: Distribution of week wise granulation tissue formation in the study.

	Normal saline		Papaya			
Time point	**N**	**Mean**	**N**	**Mean**	**Difference**	**p-value**
Baseline	32	12.25	37	12.3514	-0.1014	0.9013
Week 1	50	26.92	50	33.66	-6.74	0.0008
Week 2	50	46.82	50	59.22	-12.4	<.0001
Week 3	50	66.66	50	81.9	-15.24	<.0001
Week 4	50	85.9	41	95.0976	-9.1976	<.0001
Week 5	40	97.55	16	98.875	-1.325	0.2704

Table 10: Distribution of reduction of ulcer size in the study.

	Normal saline		Papaya			
Time point	**N**	**Mean**	**N**	**Mean**	**Difference**	**p-value**
Week 1	31	0.9087	34	0.8929	0.0158	0.8858
Week 2	49	1.4339	49	1.63	-0.1961	0.3065
Week 3	50	2.1564	50	2.5062	-0.3498	0.2158
Week 4	50	3.0306	50	3.6966	-0.666	0.0866

Table 11: Slough/necrotic tissue reduction in diabetes vs non-diabetes patients in papaya group.

Diabetes status	Time point	N	Mean	Std.	Minimum	Maximum	Difference from baseline	p-value
Yes	Baseline	30	63.5333	12.0594	32	84		
	Week 1	30	43.1	10.2363	21	68	-20.4333	<0.0001
	Week 2	30	28.2667	9.3769	8	43	-35.2667	<0.0001
	Week 3	24	15.6667	5.3703	10	34	-50.75	<0.0001
	Week 4	2	10.5	0.7071	10	11	-61	0.0521
No	Baseline	20	64.75	11.2712	42	78		
	Week 1	20	41	8.8139	26	54	-23.75	<0.0001
	Week 2	20	21.8	7.0233	12	33	-42.95	<0.0001
	Week 3	9	15.2222	3.4197	11	20	-52.6667	<0.0001
	Week 4	0						

Table 12: Distribution of granulation tissue formation in diabetes vs non-diabetes patients in papaya group.

Diabetes status	Time point	N	Mean	Std.	Minimum	Maximum	Difference from baseline
Yes	Baseline	23	12.1304	3.8412	6	19	
	Week 1	30	32.1667	11.0706	12	57	24.3913
	Week 2	30	56.9667	11.4786	34	79	48.4783
	Week 3	30	78.6667	10.8924	56	100	68.087
	Week 4	28	94.2143	7.4851	79	100	82.8571
	Week 5	12	98.5	3.5291	90	100	89.3333
No	Baseline	14	12.7143	2.9982	8	19	
	Week 1	20	35.9	12.0783	14	58	28.5
	Week 2	20	62.6	11.2034	42	78	52.2143
	Week 3	20	86.75	11.5434	60	100	75.0714
	Week 4	13	97	4.761	88	100	82.25
	Week 5	4	100	0	100	100	87.75

Table 13: Reduction of ulcer size in diabetes versus non-diabetes patients in papaya dressing.

Diabetes Status	Time point	N	Mean	Std.	Minimum	Maximum	t-value
Yes	Week 1	20	0.964	0.4304	0.41	2.11	10.02
	Week 2	29	1.709	1.0265	0.4	4.37	8.97
	Week 3	30	2.6383	1.5577	0.5	7.32	9.28
	Week 4	30	3.919	2.1519	0.86	10.12	9.98
No	Week 1	14	0.7914	0.365	0.32	1.54	8.11
	Week 2	20	1.5155	0.9152	0.32	3.16	7.41
	Week 3	20	2.308	1.4357	0.84	5.27	7.19
	Week 4	20	3.363	2.0424	1.12	8.31	7.36

Table 14: Percentage reduction in slough/necrotic tissue from baseline.

	Normal saline		Papaya			
Time point	**N**	**Mean**	**N**	**Mean**	**Difference**	**p-value**
Week 1	50	-26.7402	50	-33.8116	7.0714	0.0001
Week 2	50	-48.0757	50	-60.011	11.9353	<0.0001
Week 3	50	-68.8044	50	-84.4574	15.6531	<0.0001
Week 4	50	-86.7518	50	-99.4085	12.6567	<0.0001

In the second week comparison p-value was 0.049, third week it was 0.0003 and the fourth week it was 0.0082. Papaya group showed better slough reduction in 2nd, 3rd and 4th weeks compared to normal saline (Table 8).

Week wise comparison between the two groups showed that papaya showed better granulation tissue formation after 2nd, 3rd and 4th weeks when compared to normal saline group. p-value was less than 0.0001 at the end of 4th week (Table 9). Week wise comparison of reduction in size of ulcer of ulcer did not show any significant difference (Table 10).

There was no significant difference in reduction of slough/necrotic tissue between diabetes and non-diabetes patients (Table 11). There was no significant difference in formation of granulation tissue between diabetic and non-diabetic patients (Table 12).

There was no significant reduction in ulcer size between diabetic and non-diabetic patients (Table 13). There was significant difference in percentage reduction in slough necrotic tissue in papaya group compared to normal saline group (Table 14). Disappearance of slough/necrotic tissue was more significant in papaya group in 3rd and 4th week when compared to normal saline group (Table 15).

Table 15: Reduction in slough/necrotic tissue.

Complete disappearance of slough tissue	Normal saline	Papaya	p-value (fisher exact test)
	N (%)	N (%)	
Week 3			
Yes	1 (2.0)	17 (34.0)	<0.0001
No	49 (98.0)	33 (66.0)	
Week 4			
Yes	18 (36.0)	48 (96.0)	<0.0001
No	32 (64.0)	2 (4.0)	

At third month follow up showed 78% of wounds treated with papaya were completely healed and 22% were healing. 72% of wounds treated with normal saline were completely healed and 28% were healing (Table 16).

Table 16: Mean follow up among the study group after 3 months.

Status	Dressing			Chi-square	p-value
	Normal saline	Papaya	Total		
Healed	36	39	75	0.48	0.4884
	72%	78%			
Healing	14	11	25		
	28%	22%			
Total	**50**	**50**	**100**		

22 patients underwent SSG in normal saline group and 19 patients in papaya group. 5 patients underwent secondary suturing in normal saline group and 4 patients in papaya group. 23 patients in normal saline group and 27 patients in papaya group did not require any additional treatment (Table 17).

Table 17: Additional treatment: SSG/secondary suturing.

Additional treatment	Dressing		
	Normal saline	Papaya	Total
Healed	23	27	50
	46%	54%	
SSG	22	19	41
	44%	38%	
Sec. Suturing	5	4	9
	10%	8%	
Total	**50**	**50**	**100**

DISCUSSION

Enzymatic chemical debriding agents like collagenase, pure papain and papain urea combinations have been in practice for wound bed preparation. Enzymatic debridement with papaya is a cost effective, easily available and is eco-friendly also.

Present study results have shown that there is significant difference (p-value<0.001) in granulation tissue formation with papaya dressing when compared to normal saline dressing in third and fourth weeks. This is attributed to granulation tissue formation induced by Papain and chymopapain. Slough reduction with papaya was also significant, as 96% of the patients were completely cleared of slough at the end of fourth week, when compared to 36% with normal saline dressing. The p- value was (0.0082) significant during second, third and fourth week of the papaya dressing.

There was no significant reduction in ulcer size (p-value of 0.086) when compared to normal saline. Reductions in ulcer size in both groups were similar. In well controlled diabetes mellitus, papaya can be used as a debriding agent safely. Wet to dry normal saline dressings is routinely employed for wound dressings, as it is cost effective and easily available. But in comparison to papaya it takes a longer duration for healing and time consuming. There were no hypersensitivity, tolerability or side effects in both the groups, as previous studies have already confirmed the safety and tolerability aspects of papaya. Patient has to be clearly instructed to use semi ripe papaya since raw papaya application is associated with pain.

Limitations of this study are related to lack of standardized methods of papaya preparation. The

enzymatic content of papaya is said to decrease as fruit ripens, suggesting a better efficacy in semi ripe papaya. In spite of difference in enzyme content as the fruit ripens, previous studies confirm that there is no difference is in antibacterial activity in ripe and unripe fruit.

Papaya dressing can be encouraged as papaya is easily available in India throughout the year and cost effective also. Thus, in terms of efficacy, papaya dressing can be a good and better dressing method compared to normal saline dressing.

Papaya induces development of healthy granulation tissue, as the fruit is rich in vitamin C which helps in conversion of proline to hydroxyproline which is a specific indicator of collagen content laid during wound healing.[5] It doesn't act on normal tissue as it acts only on tissues lacking α-1 antitrypsin plasmatic antiprotease that inhibits proteolysis in healthy tissues.[4] Papaya extract breaks down the biofilm defences, as this biofilm gives protection to bacteria from ultraviolet rays and oxygenation. Bacteria in chronic wounds live within these biofilm communities protecting them from host immune response.[6] Other preparation in the market is papain urea chlorophylline copper complex which acts by inhibiting hemaglutination, inflammatory properties of protein degradation and decreases pain and wound odour.[7]

The wound healing property of papaya is attributed to the endolytic plant enzyme papain.[8] Latex from raw papaya fruit is rich in papain. Papain has a preference to cleave peptide bonds involving basic amino acids and in particular arginine and lysine.[9] Latex of *Carica papaya* fruit contains four cysteine endopeptidases namely papain, chymopapain, glycyl endopeptidase and carcain (a papaya endopeptidase-II).[10]

CONCLUSION

Papaya dressing is a better enzymatic agent when compared to wet to dry normal saline mechanical debridement. Papaya dressing was found to remove slough and necrotic tissue more rapidly when compared to normal saline as per present study. Wounds treated with papaya dressing had a faster granulation tissue formation compared to normal saline dressing. Overall response to treatment with papaya dressing was significantly better when compared to normal saline dressing.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Hopkinsons I. Molecular components of extracellular matrix. J Wound Care. 1992;1(1):52-4.
2. Locono JA, Erlich HP, Gottrup F. Wound biology and management. 1st ed. Oxford Medical Publications; 1998:10-22.
3. Young T. Debridement- Is it time to revisit clinical practice? Br J Nurs. 2011;20(11):S24-8.
4. Lopes MC, Mascarini RC, da Silva BM, Flório FM, Basting RT. Effect of a papain-based gel for chemomechanical caries removal on dentin shear bond strength. J Dent Child (Chic). 2007;74(2):93-7.
5. Starley IF, Mohammed P, Schneider G, Bickler SW. The treatment of paediatric burns using tropical papaya. Burns. 1999;25(7):636-9.
6. Edwards R, Harding KG. Bacteria in wound healing. Curren opin infect Dis. 2004;17:91.
7. Emeruwa A. Antibacterial substance from *Carica papaya* fruit extract, J Natural Prod. 1982;45:132.
8. Dawkins G, Hewitt H, Antibacterial effects of *Carica papaya* fruit on common wound organisms. West Indian Med J. 2003;52:290.
9. Menard R, Khouri HE, Plouffe C, Dupras R, Ripoll D, Vernet T, et al. Protein engineering study of role of aspartate in catalytic mechanism of papain. Biochemistry. 1990;29:6709-13.
10. Azarkan M, Looze H. Fractionation and purification of enzymes stored in latex of *Carica papaya*. J Chromatogr B. Analyst Technol. Biomed Life Sci. 2003;4(6)229-30.

Cite this article as: Vasuki V, Thanmaran NB, Vimalakaran B, Madan K. Comparative study of papaya dressing vs normal saline dressing in healing of ulcers. Int Surg J 2017;4:1209-16.