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AN EXPERIMENTAL STUDY TO ASSESS THE EFFICACY OF BIODEGRADABLE PATCH IMPREGNATED WITH COMPOUND AYURVEDIC DRUG IN EXCISIONAL WOUND MODEL OF ALBINO RAT

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ABSTRACT

The aim of this study is to assess the wound healing activity of Biodegradable patch on excisional wound model in Albino Rat. Bio degradable patches were prepared by using the Compound ayurvedic drugs consisting of aqueous extracts of stem bark of four Ficus species i.e Vata (*Ficus bengalensis* Linn.),Ashwatha (*Ficus religiosa* Linn.),Udumbara (*Ficus glomerata* Roxb.),Plaksha (*Ficus lacor* Buch-Ham.) impregnated in Poly(lactic acid),and Poly Capro lactone as a polymer base. Study on animal models showed enhanced rate of wound contraction and drastic reduction in healing time than control group, which might be due to enhanced epithelialization. The animals treated with Bio degradable patch in which Compound Ayurvedic Drug was impregnated in Poly(lactic acid) as a polymer base showed significant (*p< 0.01) wound healing results when compared with control groups (dressing with Normal Saline). The treated wound after nine days itself exhibited marked dryness of wound margins with tissue regeneration. Groups treated with this patch showed better wound closure compared to control group. The cost

effective factor and biodegradation of the prepared dermal wound healing patch was also found to be significant.

KEYWORDS: Bio degradable patch, ficus species**,** excision wound model, wound healing.

INTRODUCTION

A wound may be defined as a break in the epithelial integrity of the skin or may also be defined as a loss or breaking of cellular anatomic or functional continuity of living tissue.[1] Proper healing of wounds is essential for the restoration of disrupted anatomical continuity and disturbed functional status of the skin.[2] Healing is a complex process initiated in response to an injury that restores the function and integrity of damaged tissues. Wound healing involves continuous cell-cell and cell-matrix interactions that allow the process to proceed in three overlapping phase's viz. inflammation (0-3 days), cellular proliferation (3-12 days) and re modeling (3-6 months).[3] The basic principle of optimal wound healing is to minimize tissue damage, provide adequate tissue perfusion, oxygenation, proper nutrition and moist wound healing environment to restore the anatomical continuity and function of the affected part.[4] Recently several technical Advancements have been done and resulted in new techniques for drug delivery and the best-known and widely used technique for delivering drugs and medications through the skin without using needles is dermal patch technology[5]

Dermal patch means a patch containing drug substances pressed on to the skin which is non-invasive, convenient, painless, and can avoid gastrointestinal toxicity (e.g. peptic ulcer disease) and bypass the hepatic first pass metabolism.[6] These techniques are capable of controlling the rate of drug release. The drug delivery through Dermal patch has advantage to deliver medicines via skin to systemic circulation at a predetermined rate and maintain therapeutic concentration for prolong period of time. Therefore the dermal patch technology has proven to be fastest, easiest, safest and most economical way to help wound to heal.[7] The use of polymeric materials in or as drug delivery devices involves incorporation of biodegradability into the drug delivery system.[8] However, a number of degradable polymers are potentially useful for this purpose including a variety of synthetic and natural substances. Among these Poly (lactic acid) (PLA) and Poly Capro lactone (PCL) has been used worldwide as bio degradable substrate for nano drug delivery.[9] So in this study four groups were taken, Group I animals were left untreated and considered as a control group, Group II animals were treated by drug impregnated in biodegradable patch made up of Poly capro lactone(PCL), Group III animals were treated by drug impregnated in biodegradable patch

made up of Poly (lactic acid)(PLA) and Poly Capro lactone (PCL) in 50:50 ratio and Group IV animals were treated by drug impregnated in biodegradable patch made up of Poly (lactic acid) (PLA).

Preparation of Biodegradable Patch by Solvent Casting Method

In the present study aqueous extract of all four drugs (CAD) were together grinded and the powdered drug were put through sieve no. 100 to fix the particle size of drug to 100 micron. Poly(lactic acid) polymer and Poly Capro lactone was taken with Dichloromethane solution. 25%W/W Compound Ayurvedic Drug was mixed with dichloromethane solution and kept over ultrasonicator for dispersion. After ultrasonication 25%W/W Compound Ayurvedic Drug was mixed with polymer solution and kept over rotator having 1500rpm for mixing. Standard Film applicator was taken to make the film of a standard size of 100 micron thickness. The Solution of Compound Ayurvedic drug and Polymer was pasted over glass sheet in a cold room at 4°C. The Film applicator was moved over the solution and a film of 100 micron standard thickness was made. Dichloromethane, being a volatile substance got evaporated and Bio degradable film having 25% W/W drug and polymer remained in the patch. Biodegradable patch was finally made after evaporation of the solvent. The prepared films were peeled from the plates and the films showed good film forming property (filmogenicity).

MATERIAL AND METHOD

Twelve week old healthy albino rat (150gm-200gm) of either sex were taken for the study. They were housed in standard condition (Temperature 22±2degree centigrade, R.H.60±5%and 12 hr light dark cycle).The animal house were sanitized with poly propylene cages containing sterile paddy husk as bedding, food and water *ad libitum*.

Excisional Wound Model

A circular wound of about 100 mm^2surface area (full thickness, completely trans dermal) were made on the pre-shaved, sterile (wiped with 70% alcohol) over dorsal thoracic region of mice. All surgical procedures were carried out under thiopentone sodium (25 mg/kg, i.p.) anaesthesia.[10] The animals were divided in 4 groups comprising of 6 mice in each group.

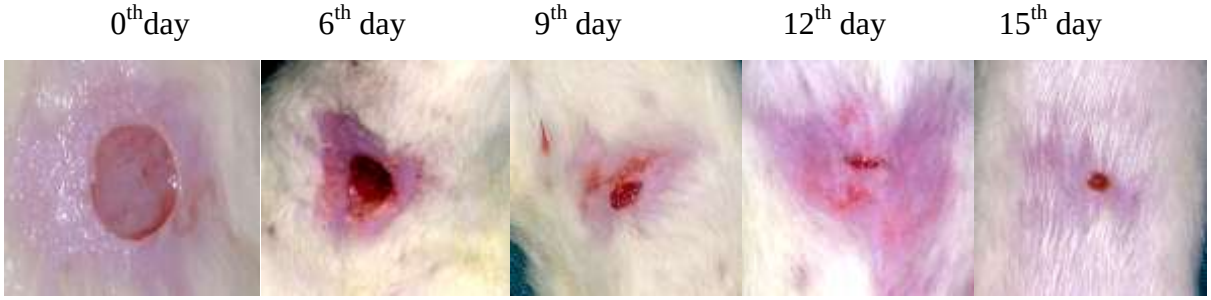
Animals of Group I were left untreated and dressing was done with Normal Saline considered as a control group.

Animals of Group II were treated by drug impregnated in biodegradable patch made up of Poly Capro lactone(PCL).

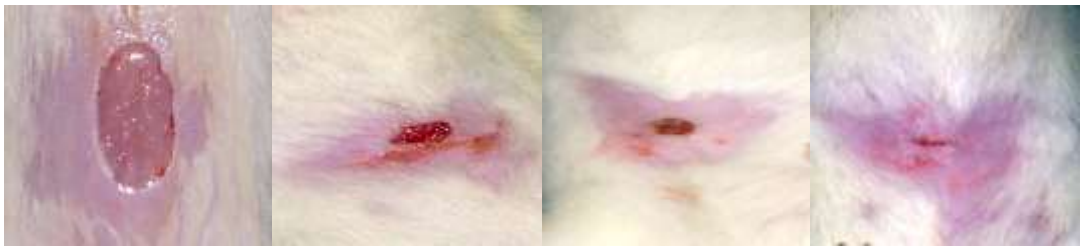
Animals in Group III were treated by drug impregnated in biodegradable patch made up of Poly (lactic acid)(PLA) and Poly Capro lactone (PCL) in 50:50 ratio.

Animals in Group IV were treated by drug impregnated in biodegradable patch made up of Poly (lactic acid) (PLA).

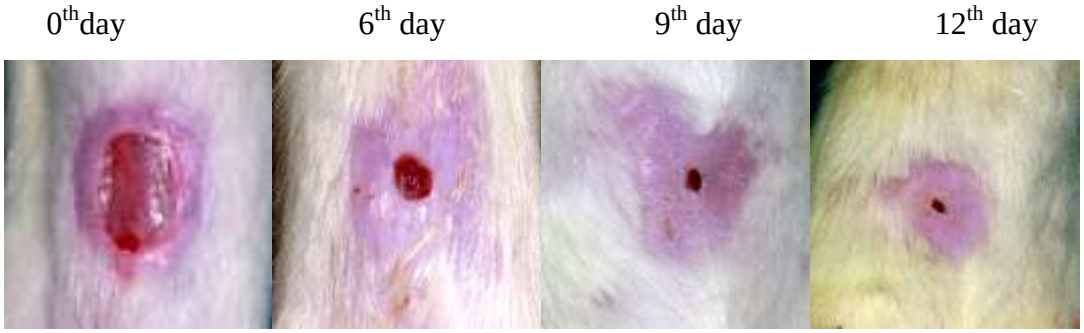
Control group



PCL group



PLA+PCL(50:50) group



PLA group

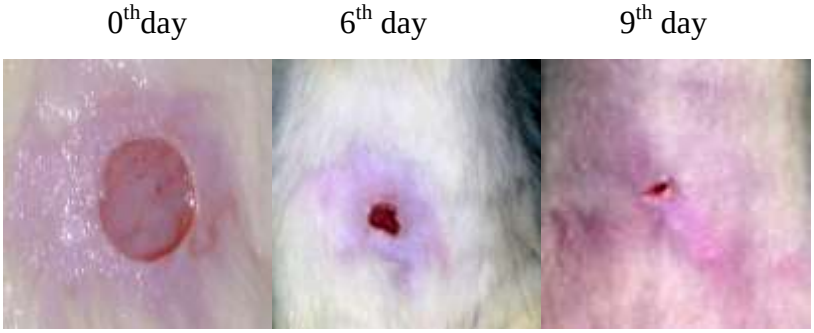


Table 1. Surface area

Group		Surface area (Mean ± S.D.)				
		Day 3	Day 6	Day 9	Day 12	Day 15
Group I Control		0.543 ± 0.16	0.396 ± 0.21	0.290 ±0.014	0.145 ± 0.018	0.016 ± 0.008
Group II PCL		0.510 ± 0.020	0.356 ± 0.20	0.233 ± 0.016	0.085 ± 0.0104	0.00 ± 0.00
Group III PLA-PCL		0.428 ± 0.026	0.291 ± 0.019	0.135 ± 0.013	0.0100 ± 0.006	-
Group IV PLA		0.390 ± 0.23	0.191 ± 0.019	0.015 ± 0.008	-	-
Between the group comparison One Way ANOVA		F = 61.51 P=0.00	F = 116.721 P=0.00	F = 480.55 P=0.00	F = 164.70 P=0.00	F = 25.00 P=0.001
Post Hoc Gr I vs othergroups Dunnett test	I vs II	0.044	0.007	0.000		
	I vs III	0.000	0.000	0.000		
	I vs IV	0.000	0.000	0.000		

In group I surface area was reduced from 0.543 ± 0.16 on day 3rd to 0.016 ± 0.008on 15th day. Total reduction in surface area was 0.535 ± 0.16mm^2(Table 1,Figure1) in 15 days. The reduction in surface area on 9th day was 46% and was 97%on 15th day.

In group II surface area was reduced from 0.510 ± 0.020 on day 3rd to 0.00 ± 0.00 on 15th day. Total reduction in surface area was 0.510 ± 0.02 mm^2 (Table 1,Figure1). The reduction in surface area on 9th day was 51% and was 78%on 12th day.

In group III surface area was reduced from 0.428 ± 0.026 on day 3rd to 0.0100 ± 0.006 on 12th day. Total reduction in surface area was0.427 ± 0.026 mm^2(Table 1,Figure1).The reduction in surface area on 9th day was 68% and was 97%on 12th day.

In group IV surface area was reduced from 0.390 ± 0.23 on day 3rd to 0.015 ± 0.008 on 9th day.Total reduction in surface area was 0.375 ± 0.16 mm^2(Table 1,Figure1).The reduction in surface area on 9th day was 96% .

Figure-1 Surface area

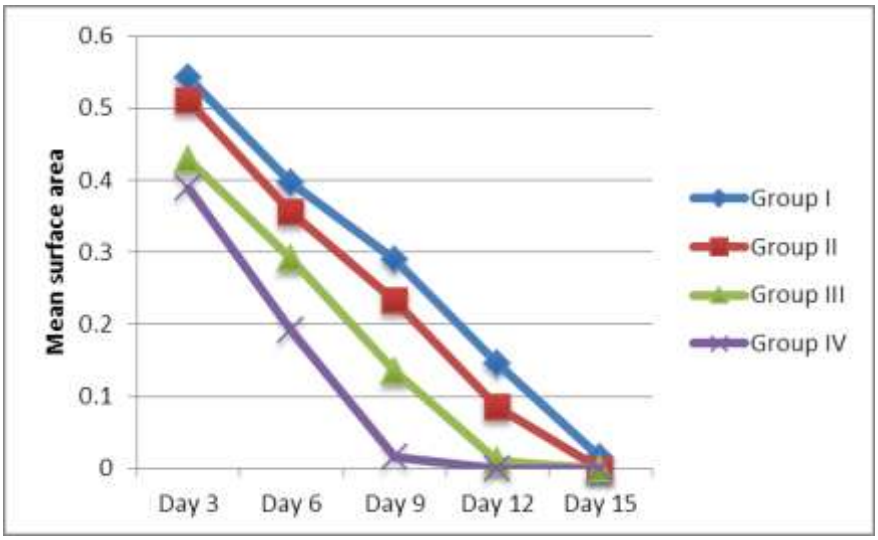


Figure 1; Group I Control; Group II PCL; Group III PLA-PCL; Group IV PLA

Table 2. Unit Healing Time

Group		UHT (Mean ± S.D.)				
		1	2	3	4	5
Group I control		29.60 ± 1.152	24.28±0.749	25.01±1.23	22.00±0.901	21.32 ± 0.801
Group II PCL		21.08 ± 1.132	22.10±0.945	22.56±1.01	19.66±2.03	0.00 ± 0.00
Group III PLA-PCL		14.95 ± 0.75	19.53±0.845	19.11±0.783	18.68±1.09	0.00 ± 0.00
Group IV PLA		10.53 ± 1.03	14.68±0.507	14.20±1.17	0±0.0	-
Between the group comparison One Way ANOVA		F = 384.98 P=0.000	F = 169.36 P=0.000	F = 116.20 P=0.000	F = 402.99 P=0.00	F = 424.9 P=0.001
Post Hoc Gr I vs other groups Dunnett test	I vs II	0.000	0.000	0.000	0.011	
	I vs III	0.000	0.000	0.000	0.000	
	I vs IV	0.000	0.000	0.000	0.000	

In group I Unit healing time reduced from 29.60 ± 1.152 on day 3rd to 21.32 ± 0.801 on 15th day. Total reduction in Unit healing time was 08.28 ± 0.801(Table 2, Figure 2).

In group II, Unit healing time reduced from 21.08 ± 1.132 on day 3rd to 0.00 ± 0.00 on 15th day. Total reduction in Unit healing time was 21.08 ± 1.132 (Table 2, Figure 2).

In group III, Unit Healing Time reduced from 14.95 ± 0.75 on day 3rd to 0.00 ± 0.00 on 15th day. Total reduction in Unit healing time was 14.95 ± 0.75(Table 2, Figure2).

In group IV, Unit healing time reduced from 10.53 ± 1.03 on day 3rd to 0.00 ± 0.00 on 12thday. Total reduction in Unit healing time was 10.53 ± 1.03(Table 2, Figure 2).

Figure- 2 Unit Healing Time

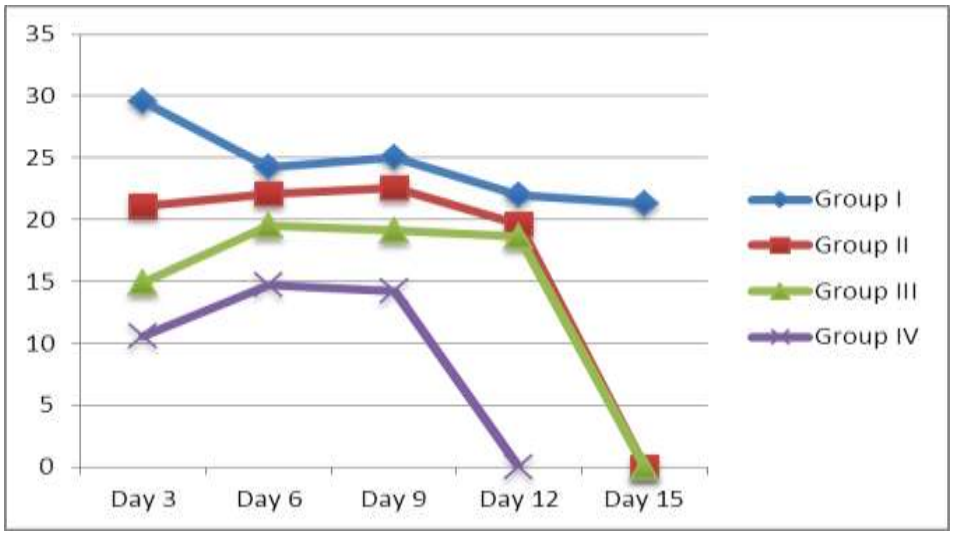


Figure 2: Group I Control; Group II PCL; Group III PLA-PCL; Group IV PLA

DISCUSSION

Surface area of wound was significantly reduced in group IV on 9th day rather than group I,II, III. This proves that healing property of biodegradable patch in which poly (lactic acid) taken as a substrate for impregnation of compound ayurvedic drug was more effective in comparison to groups I,II,III (Table 1,Figure1).The average Unit healing time was found significantly low in Group IV on 12th day in comparison to Groups I,II and III. This proves healing property of biodegradable patch in which poly (lactic acid) taken as a substrate for impregnation of compound ayurvedic drug was more effective in comparison to other groups(Table 2,Figure 2).

CONCLUSION

Study on excisional wound models showed enhanced rate of wound contraction and drastic reduction in healing time than control, which might be due to enhanced healthy epithelialization. The animals treated with biodegradable patch in which poly (lactic acid) taken as a substrate for impregnation of compound ayurvedic drug showed significant ($p< 0.01$) results when compared with control and other groups. The treated wound in Group IV after nine days exhibited marked granulation tissue regeneration.

Topical route of application has a great potential as an effective and safe way to administer in the form of biodegradable patch in which poly (lactic acid) taken as a substrate for impregnation of compound Ayurvedic drug for local wound healing activity. Preliminary tests of skin irritation in albino rats indicates negligible systemic absorption and side effects.

Hence a clinical trial on patients of wound may be performed to assess efficacy of Biodegradable patch.

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