International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 9, Issue 8, 2017

Original Article

USE OF CASHEW BARK EXUDATE GUM IN THE PREPARATION OF 4 % LIDOCAINE HCL TOPICAL GELS

M. SAQUIB HASNAIN[1], POONAM RISHISHWAR[1*], SADATH ALI[2]

[1]Department of Pharmacy, Shri Venkateshwara University, NH-24, Rajabpur, Gajraula, Amroha 244236, U. P., India, [2]Department of Pharmacy, Glocal University, Saharanpur 247001,U. P., India
Email: prishishwar@gmail.com

Received: 09 May 2017 Revised and Accepted: 19 Jun 2017

ABSTRACT

Objective: The objective of the current work was to prepare and evaluate *ex vivo* skin permeation of cashew bark exudate gum based 4 % lidocaine HCl topical gels.

Methods: In the current work, 4 % lidocaine HCl topical gels were prepared by using different concentrations of cashew bark exudate gum, HPMC K4M, lidocaine HCl, methyl paraben (as preservative) and glycerin (as plasticizer). The formulated topical gels were evaluated for pH, viscosity, and *ex vivo* skin permeation through excised porcine ear skin membrane.

Results: The pHs of these formulated 4 % lidocaine HCl topical gels were found within the range of 6.04±0.02 to 6.52±0.04; whereas, the viscosities were measured within the range, 4.38±0.02 x $10^6$to 4.74±0.04 x 10^6 cps. Sustained *ex vivo* permeation of lidocaine was measured over 7 h. Highest *ex vivo* permeation flux was measured when 0.1 % menthol was incorporated as a permeation enhancer. It was also higher than that of the marketed 4 % lidocaine HCl topical gel. The stability study by freeze thaw cycle method revealed physically stable gels without the occurrence of syneresis.

Conclusion: The results clearly indicate a promising potential of the use of cashew bark exudate gum as a gelling material with HPMC K4M to prepare 4 % lidocaine HCl topical gels of good skin permeation capability.

Keywords: Cashew bark exudate gum, Gel, Lidocaine HCl, Skin permeation, Topical application

DOI: http://dx.doi.org/10.22159/ijpps.2017v9i8.19815

INTRODUCTION

During past few decades', topical drug delivery through the skin has been employed as a safe and effective way to deliver drugs for local and sustained actions [1-6]. As compared to oral drug delivery, it restricts systemic absorption and hepatic metabolism of drugs, avoids the chances of gastrointestinal irritation and also, minimises systemic toxicities [7-9]. The therapeutic effectiveness of topical drug delivery formulations mostly depends on the capability to deliver drugs to the sites of action onto skin surface [9-11]. In general, local anaesthetics are administered through parenteral routes (mainly, intravenous and hypodermic routes) [12]. Only, a few local anaesthetics are applied topically, by the dermatologists and the dentists, mainly [13]. The topical applications of local anaesthetics facilitate some potential benefits over parenteral routes such as continuous drug delivery, avoidance of systemic side-effects (like hematoma and nerve damages) and thus, improvement of patient compliances [14]. However, the topical delivery of local anaesthetics is associated with some constraints like poor skin permeability and slow skin penetration rates. Therefore, effective topical formulations of local anaesthetics with good skin permeability and rapid skin penetration rates are desperately essential.

Lidocaine is a local anaesthetic, which is employed in the treatment of open skin lesions and sores [15]. It is also employed as a topical local anaesthetic in various small surgical procedures like venipuncture, suturing of wounds, *etc* [16]. The topical application of lidocaine recommends some potential benefits such as rapid onset of action, minimum systemic toxicity, *etc* [17]. These benefits favour the topical delivery of lidocaine for local action. In the previous literature, a few topical formulations of lidocaine are reported [18-22]. In the current research, we made an attempt to prepare 4 % lidocaine HCl topical gels of using cashew bark exudate gum.

Cashew bark exudate gum is a natural polymer extracted from *Anacardium occidentale* tree, belonging to the family: Anacardiaceae [23-24]. This plant derived gum molecules are composed of galactose unit-chains of with branches of glucose, arabinose, rhamnose and uronic acid units [25-26]. According to the previous literature, a flurry of the investigation was performed on the utilizations of cashew bark exudate gum as pharmaceutical excipients, such as, tablet binder in paracetamol tablets [27], mucoadhesive in the buccal formulation of curcumin [28] and gelling agent in aceclofenac gel [29]. In the present research, cashew bark exudate gum and hydroxypropyl methylcellulose (HPMC K4M) was employed as a gelling agent in the formulation of lidocaine HCl topical gels. *In vitro* skin permeability of lidocaine through the excised porcine ear skin membrane from the formulated 4 % lidocaine HCl topical gels were also tested and analyzed.

MATERIALS AND METHODS

Materials

Lidocaine HCl (Albert-David Pvt. Ltd., India), HPMC K4M (Loba Chemie Pvt. Ltd., India), menthol (Qualigens Fine Chemicals, India) were used. Cashew bark exudate gum was extracted from the crude exudate of cashew tree bark (collected at Jharpokharia, Odisha, India in the month of September 2015). All the other chemicals and reagents used were of analytical grade and commercially available.

Extraction of cashew gum

The crude cashew bark exudate was cleaned by removing bark pieces and further extraneous substances. The crude exudate was dried in a tray drier at 50±2 °C for 10 h until it became brittle. The dried exudate was reduced to powder through milling in a domestic blender and then, sieving. 1 kg of the crude cashew bark exudate powder was dissolved in 2 liter distilled water and the exudate solution was boiled for 1 hour under occasional stirring in a temperature controlled water-bath. After cooling at room temperature, the resulting exudate solution was further cooled by keeping in a refrigerator overnight to settle out proteins and

undissolved materials, if occurred. The upper solution was decanted and then, concentrated at 50±2 °C by a temperature controlled water-bath to 1/3rd of its original volume. After cooling the concentrated cashew tree exudate solution at room temperature, it was poured into twice the volume of acetone with continuous stirring. The formed precipitate was filtered and washed repeatedly with acetone. The collected precipitate was dried in a tray drier at 50±2 °C for 10 h. The obtained dried film of precipitate was milled to a fine powder of cashew gum and sieved through sieve number 80. The extracted cashew tree bark exudate gum was kept in an air-tight desiccator until further use.

Preparation of 4 % lidocaine HCl gels

4 % Lidocaine HCl gels were prepared by using different concentrations of cashew bark exudate gum, HPMC K4M, lidocaine HCl, methyl paraben (as a preservative) and glycerin (as plasticizer). The formula of 4 % lidocaine HCl gels is shown in table 1. The formulated gels were stored in a cool place until further use.

pH determination

pHs of formulated 4 % lidocaine HCl gels were determined using a pH meter (Systronics Instruments, India) by inserting glass electrode into the gel, completely [22].

Viscosity measurement

Viscosities of formulated 4 % lidocaine HCl gels were measured using a cone and plate viscometer (Brookfield DV III Ultra V6.0 RV, Brookfield Engineering Laboratories, Middle-boro, MA) at 25±0.3 °C. Rheocalc V2.6 software was employed for the calculation of viscosities [22].

Table 1: Formulation charts of 4 % lidocaine HCl topical gels containing cashew bark exudate gum

Ingredients	Formulation codes			
	G1	G2	G3	G4
Lidocaine HCl (%)	4	4	4	4
Cashew bark exudate gum (%)	5.5	6	6.5	6.5
HPMC K4M (%)	2	2	2	2
Menthol (%)	-	-	-	0.1
Propylene glycol (%)	5	5	5	5
Methyl paraben (%)	0.02	0.02	0.02	0.02
Purified water q. s. (gm)	10	10	10	10

Preparation of skin for *ex vivo* permeation experiment

Excised porcine skin membrane was employed for the *ex vivo* permeation [2-3]. The porcine ear skin was collected from slaughterhouse after sacrificing the animal within 1 hr. The hair onto skin surface was taken out by means of a hair clipper and afterwards, the full thickness of the skin was collected. The fatty layers sticking to the dermis side of the skin was eradicated by means of a surgical scalpel. Finally, these excised porcine ear skin membranes were thoroughly cleaned through rinsing with distilled water and used.

***Ex vivo* skin permeation experiment of 4 % lidocaine HCl gels**

Ex vivo skin permeation of lidocaine from various formulated 4 % lidocaine HCl gels and marketed 4 % lidocaine HCl gel was performed by means of Franz diffusion cell. The Franz diffusion cell comprises 2 chambers: the donor chamber and the receptor chamber [22]. The diffusion area of the Franz diffusion cell was 0.79 cm2. The donor chamber was open at the top and was exposed to the atmosphere. The excised porcine ear skin membrane was mounted in between the chambers of the cell with stratum corneum facing the donor chamber and clamped into the position. A magnetic stirrer bar was fitted inside the receptor chamber, which was filled with phosphate buffer saline (PBS, pH 7.4) as receptor phase medium. A small concentration of sodium azide (0.0025 % w/v) was put into the system to prevent the occurrence of microbial growth [30-31]. The whole system was positioned over a magnetic stirrer at 37±0.7 °C. At the start, the skin membrane was left in the Franz diffusion cell for 2 h so as to make possible hydration of the skin membrane. After 2 h of hydration of the skin membrane, 1 gm of 4 % lidocaine HCl gels was applied onto the skin membrane surface. 1 ml of receptor phase medium was collected from the receptor chamber at predetermined intervals and the same amount of fresh receptor phase medium was replaced to the receptor chamber. The amount of drug permeated through the excised porcine ear skin membrane was determined by means of a UV-VIS spectrophotometer (Shimadzu, Japan) at 274 nm of wavelength.

Skin permeation data analysis

Permeation flux

The drug amounts permeated through excised porcine ear skin membrane from various formulated 4 % lidocaine HCl gels and marketed 4 % lidocaine HCl gel were plotted against the function of time. The slopes of the linear portion of the plots were derived through regression analyses. The permeation fluxes were calculated as the slope divided by the surface area of skin membrane employed [32]:

$J_{ss} = (dQ/dt)_{ss} \cdot 1/A$, where J_{ss} is the steady state permeation flux (µg/cm²/hr), *A* is the surface area of skin membrane employed (cm²), and $(dQ/dt)_{ss}$ is the amount of drug permeated through the excised porcine ear skin membrane per unit time at a steady state (µg/hr).

Kinetics

The drug permeation data were assessed by means of some important mathematical models [33]: Zero order model: $F = K_o t$; First order model: $\ln (1 - F) = - K_1 t$; Higuchi model: $F = K_H t^{1/2}$ and Korsmeyer-Peppas model: $F = K_p t^n$, where F = fraction of drug permeated in time t, K_o = Zero order rate constant, K_1 = First order rate constant, K_H = Higuchi model rate constant, K_p = Korsmeyer-Peppas model rate constant, and n = diffusion exponent.

Stability testing

Stability testing of formulated 4 % lidocaine HCl gels was carried out using freeze-thaw cycling method [34]. The temperature of the study was varied every 24 h in between 25 °C and-5 °C for complete 5 cycles. Gel samples were scrutinised for the physical stability and syneresis.

Statistical analysis

The data were analysed with simple statistics using Bio Stat version 2009 for Windows software, Analyst Soft Inc.

RESULTS AND DISCUSSION

Preparation of 4 % lidocaine HCl gels

Lidocaine HCl (4 %) gels were formulated by using different concentrations of cashew bark exudate gum along with HPMC K4M as a gelling agent. In these formulated 4 % lidocaine HCl gels, methyl paraben and glycerine were added as preservative and plasticizer, respectively (table 1). These formulated 4 % lidocaine HCl gels were assessed for pH, viscosity, and *ex vivo* skin permeation of drug through excised porcine ear skin membrane.

pH

For a topical gel formulation, pH is important. The more acidic or basic pH of the topical formulations can change the skin

environment, which can produce skin irritation upon application [22]. The pH of all these 4 % lidocaine HCl gels containing cashew bark exudate gum was measured within the range of 6.04±0.02 to 6.52±0.04 (table 2), demonstrating that these gels were close to normal pH of the skin and can be used topically.

Viscosity

The viscosities of these formulated 4 % lidocaine HCl gels containing cashew bark exudate gum were determined at 25±0.3 °C, which ranges in between, 4.38±0.02 x $10^6$to 4.74±0.04 x 10^6 cps (table 2). All these gels demonstrated a pseudoplastic flow (indicative of share thinning). This kind of rheology of these gels is ideal for topical formulations [34].

***Ex vivo* permeation**

The formulated 4 % lidocaine HCl gels containing cashew bark exudate gum and marketed topical gel formulation of 4 % lidocaine HCl were evaluated for *ex vivo* permeation through excised porcine ear skin membrane. The *ex vivo* skin permeations of lidocaine from the formulated and marketed topical gels were observed to be sustained over a period of 7 h (fig. 1). The *ex vivo* skin permeation flux (µg/cm²/hr) values for all these topical gels through the excised porcine ear skin membrane were shown in table 3. The results of *ex vivo* skin permeation experiment of 4 % lidocaine HCl gels illustrated permeation fluxes within the range, 836.42±10.78 to 1538.38±14.03 µg/cm²/hr. The permeation flux values were found to be increased with the increment of HPMC K4M amounts within the gel formula.

Table 2: pHs and viscosities of 4 % lidocaine HCl topical gels*

	Formulation codes			
	G1	**G2**	**G3**	**G4**
pH	6.04±0.02	6.24±0.04	6.52±0.04	6.48±0.03
Viscosity x 10^6 (cps)	4.38±0.02	4.59±0.04	4.70±0.04	4.74±0.04

*(mean±standard error, n = 3)

Highest *ex vivo* permeation flux (1538.38±13.77 µg/cm²/hr) was measured in the case of G4 gel containing 0.1 % menthol as a permeation enhancer. 1422.18±12.76 µg/cm²/hr of ex *vivo* permeation flux was measured for the marketed topical gel of 4 % lidocaine HCl, which was higher than G3 gel and lower than G4 gel (containing 0.1 % menthol). Menthol (a permeation enhancer terpene derivative) has long been employed as an effective permeation enhancer in numerous topical gels [8, 35]. The skin permeation enhancers are the materials aiding absorption of drugs across the skin barrier through raising the permeability of the skin, temporarily. The skin permeation enhancers are mainly working through one or more of these 3 mechanisms: (a) improved partition of drug or solvent into stratum corneum, (b) disruption of the highly-ordered stratum corneum lipid structure and (c) interaction with the intracellular-proteins [35]. As skin permeation enhancer, menthol preferentially distributes into the intercellular spaces of the stratum corneum [36]. In addition, menthol perhaps produces reversible disruption of lipid domains of the stratum corneum and thus, enhances the permeation of drugs through the skin [22].

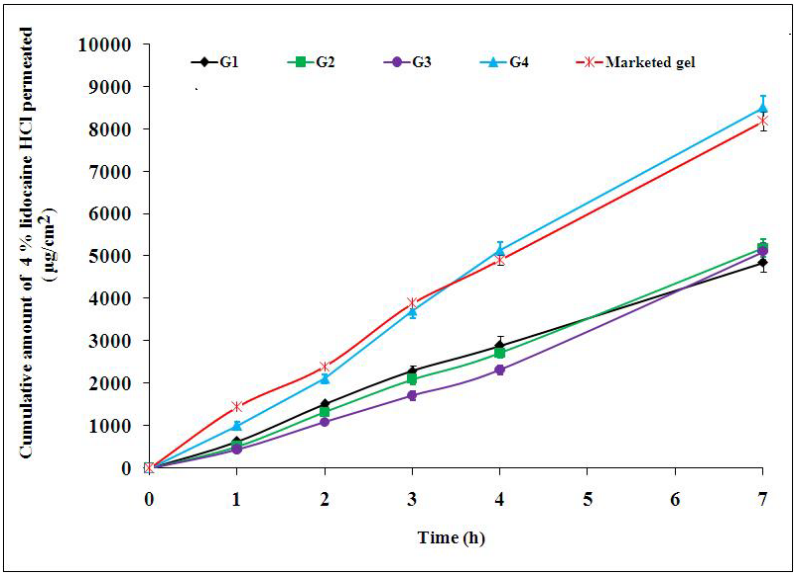

Fig. 1: *Ex vivo* permeation profile through excised porcine ear skin membrane per unit area from 4 % lidocaine HCl topical gels (mean±standard error, n = 3)

Table 3: *Ex vivo* permeation fluxes (J, µg/cm²/h) of 4 % lidocaine HCl topical gels

Formulation code	Permeation flux (J, µg/cm²/h)*
G1	836.42±10.78
G2	992.76±9.12
G3	1236.08±11.70
G4	1538.38±13.77
Marketed gel	1422.18±12.76

*(mean±standard error, n = 3)

The results of *ex vivo* skin permeation from formulated topical gels containing cashew bark exudate gum and marketed topical gel of 4 % lidocaine HCl through excised porcine ear skin membrane were kinetically evaluated and analyzed using various kinetic models: zero order, first order, Higuchi, and Korsmeyer-Peppas model (table 4). When the respective correlation coefficients (R^2) were compared, Korsmeyer-Peppas model was found as a best-fit model (R^2 = 0.9957 to 0.9982) over a period of 7 h. Besides, zero order model was also found to be almost closer to the best-fit Korsmeyer-Peppas model. Again, the Korsmeyer-Peppas model was employed in the *ex vivo* lidocaine HCl skin permeation behavior analysis of these formulations: Fickian (nonsteady) when $n \leq 0.5$, case-II transport (zero order) when $n \geq 1$, and non-Fickian (anomalous) when the value of n is in between 0.5 and 1 [30-31]. The calculated diffusion exponent (*n*) values of formulated 4 % lidocaine HCl topical gels containing cashew bark exudate gum (G1 to G4) were ranged within 0.95 and 1.12 (table 4). On the other hand, n value of 0.88 was calculated for the marketed topical gel of 4 % lidocaine HCl. These results indicated that the *ex vivo* lidocaine HCl skin permeation from these formulated 4 % lidocaine HCl topical gels containing cashew bark exudate gum (G1 to G4) followed the super case-II transport mechanism.

Table 4: Curve fitting results of the *ex vivo* skin permeation of 4 % lidocaine HCl topical gels

Formulation code	G1	G2	G3	G4	Marketed gel
Zero order model	0.9886	0.9903	0.9907	0.9889	0.9926
First order model	0.8846	0.9013	0.9643	0.8607	0.8839
Higuchi model	0.7814	0.6539	0.5715	0.6524	0.7844
Korsmeyer-Peppas model	0.9963	0.9957	0.9968	0.9960	0.9982
n (diffusion exponent)	0.95	1.08	1.17	1.12	0.88

Stability

The stability of the formulated 4 % lidocaine HCl topical gels containing cashew bark exudate gum (G1 to G4) was determined by freeze thaw cycling method. The stability study by freeze thaw cycling revealed that these formulated topical gels were physically stable. However, syneresis (spontaneous contraction of gel exuding some of the fluid medium) was not observed, even after completion of 5 complete freeze thaw cycling.

CONCLUSION

4 % lidocaine HCl topical gels were prepared by using different concentrations of cashew bark exudate gum, HPMC K4M, lidocaine HCl, methyl paraben (as a preservative) and glycerin (as plasticizer). The pH of these formulated topical gels (G1 to G4) was found within the range of 6.04±0.02 to 6.52±0.04 and the viscosity was found in between 4.38±0.02 x $10^6$to 4.74±0.04 x 10^6 cps. These topical gels demonstrated sustained *ex vivo* permeation through excised porcine ear skin membrane of lidocaine HCl over a period of 7 h using Franz diffusion cell. The *ex vivo* skin permeation fluxes of these 4 % lidocaine HCl topical gels containing cashew bark exudate gum ranged 836.42±10.78 to 1538.38±14.03 µg/cm^2/hr. Highest *ex vivo* permeation flux (1538.38±13.77 µg/cm^2/hr) was measured in the case of G4 gel containing 0.1 % menthol as a permeation enhancer.

These formulated topical gels (G1 to G4) found to be best-fit with Korsmeyer-Peppas model (R^2 = 0.9957 to 0.9982) with super case-II transport mechanism over a period of 7 h. The stability study revealed that these 4 % lidocaine HCl topical gels containing cashew bark exudate gum were physically stable. Even after completion of 5 complete freeze thaw cycling, any sign of syneresis was absent in these topical gels.

ACKNOWLEDGEMENT

The authors would like to acknowledge the financial assistance provided by University Grant Commission, New Delhi, India under Maulana Azad National Fellowship for minority students as well as Shri Venkateshwara University, Gajraula, U. P, India for providing the research facility.

AUTHORS CONTRIBUTION

All authors of the current manuscript contributed equally.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Khatri SK, Rathnanand M. Formulation and evaluation of wound healing activity of linezolid topical preparations on diabetic rats. Int J Appl Pharm 2016;8:30-6.
2. Das B, Sen SO, Maji R, Nayak AK, Sen KK. Transferosomal gel for transdermal delivery of risperidone. J Drug Delivery Sci Technol 2017;38:59-71.
3. Malakar J, Basu A, Nayak AK. Candesartan cilexetil microemulsions for transdermal delivery: formulation, *in vitro* skin permeation and stability assessment. Curr Drug Delivery 2014;11:313-21.
4. Das S, Samanta A, Bose A. Design, development and evaluation of fluconazole topical gels. Asian J Pharm Clin Res 2015;8:199-206.
5. Kaur D, Raina A, Singh N. Formulation and evaluation of Carbopol 940 based glibenclamide transdermal gel. Int J Pharm Pharm Sci 2014;6:434-40.
6. Jana S, Ali SA, Nayak AK, Sen KK, Basu SK. Development and optimisation of a topical gel containing aceclofenac-crospovidone solid dispersion by "Quality by Design" approach. Chem Eng Res Des 2014;92:2095-105.
7. Verma A. Formulation and evaluation of clobetasol proprionate gel. Asian J Pharm Clin Res 2013;6:15-8.
8. Nayak AK, Mohanty B, Sen KK. Comparative evaluation of *in vitro* diclofenac sodium permeability across excised mouse skin from different common pharmaceutical vehicles. Int J PharmTech Res 2010;2:920-30.
9. Jana S, Manna S, Nayak AK, Sen KK, Basu SK. Carbopol gel containing chitosan-egg albumin nanoparticles for transdermal aceclofenac delivery. Colloids Surf B 2014;114;36-44.
10. Abdelgawad R, Nasr M, Hamza MY, Awad GAS. Topical and systemic dermal carriers for psoriasis. Int J Curr Pharm Res 2016;8:4-9.
11. Pithayanukul P, Chansri N, Sugibayashi K. The enhancing effects of common pharmaceutical solvents on the *in vitro* skin permeation of estradiol. Thai J Pharm Sci 2002;26:109-19.
12. Reiz GME, Reiz SL. EMLA–a eutectic mixture of local anaesthetics for topical anaesthesia. Acta Anaesthesiol Scand 1982;26:596–8.
13. Wang Y, Su W, Li Q, Li C, Wang H, Li Y, *et al*. Preparation and evaluation of lidocaine hydrochloride-loaded TAT-conjugated polymeric liposomes for transdermal delivery. Int J Pharm 2013;441:748-56.
14. Trotta M, Peira E, Debernardi F, Gallarate M. Elastic liposomes for skin delivery of dipotassium glycyrrhizinate. Int J Pharm 2002;241:319–27.
15. Smith DW, Peterson MR, DeBerard SC. Regional anaesthesia. Nerve blocks of the extremities and face. Postgrad Med 1999;106:57–60.
16. Lee PJ, Ahamad N, Langer R, Mitragotri S, Shastri VP. Evaluation of chemical enhancers in the transdermal delivery of lidocaine. Int J Pharm 2006;308:33-9.
17. Sarpotdar PP, Zatz JL. Evaluation of penetration enhancement of lidocaine by nonionic surfactants through hairless mouse skin *in vitro*. J Pharm Sci 1986;75:176–81.
18. Shin SC, Cho CW, Yang KH. Development of lidocaine gels for enhanced local anesthetic action. Int J Pharm 2004;287:73–8.

19. Mueller-Goymann CC, Frank SG. Interaction of lidocaine and lidocaine-HCl with liquid crystal structure of topical preparations. Int J Pharm 1986;29:147-59.
20. Padula C, S Nicoli S, Colombo P, Santi P. Single-layer transdermal film containing lidocaine: modulation of drug release. Eur J Pharm Biopharm 2007;66:422-8.
21. Rowbotham MC, Davies PS, Fields HL. Topical lidocaine gel reduces pain in post-herpetic neuralgia. Ann Neurol 1995; 37:246-53.
22. Das B, Nayak AK, Nanda U. Topical gels of lidocaine HCl using cashew gum and Carbopol 940:Preparation and *in vitro* skin permeation. Int J Biol Macromol 2013;62:514-7.
23. De Paula RCM, Rodrigues JF. Composition and rheological properties of cashew tree gum, the exudate polysaccharide from *Anacardium occidentale* L. Carbohydr Polym 1995;26:177–81.
24. Das B, Dutta S, Nayak AK, Nanda U. Zinc alginate-carboxy-methyl cashew gum micro beads for prolonged drug release: development and optimization. Int J Biol Macromol 2014;70:505-15.
25. Silva DA, de Paula RCM, Feitosa JPA, de Brito ACF, Maciel JS, Paula HCB. Carboxymethylation of cashew tree exudate polysaccharide. Carbohydr Polym 2004;58:163–71.
26. Silva DA, Feitosa JPA, Maciel JS, Paula HCB, de Paula RCM. Characterization of crosslinked cashew gum derivatives. Carbohydr Polym 2006;66:16–26.
27. Gowthamarajan K, Phani Kumar GK, Gaikward NB, Suresh B. Preliminary study of *Anacardium occidentale* gum as a binder in the formulation of paracetamol tablets. Carbohydr Polym 2011;83:506-11.
28. Gowthamarajan K, Jawahar N, Wake P, Jain K, Sood S. Development of buccal tablets for curcumin using *Anacardium occidentale* gum. Carbohydr Polym 2012;88:1177–83.
29. Kumar R, Patil MB, Patil SR, Paschapur MS. Evaluation of *Anacardium occidentale* gum as gelling agent in aceclofenac gel. Int J PharmTech Res 2009;1:695-704.
30. Malakar J, Sen SO, Nayak AK, Sen KK. Development and evaluation of microemulsions for transdermal delivery of insulin. ISRN Pharm 2011. http://dx.doi.org/10.5402/2011/780150
31. Malakar J, Nayak AK, Basu A. Ondansetron HCl microemulsions for transdermal delivery: Formulation and *in vitro* evaluation. ISRN Pharm 2012. http://dx.doi.org/10.5402/2012/428396
32. Rath Adhikari SN, Nayak BS, Nayak AK, Mohanty B. Formulation and evaluation of buccal patches for delivery of atenolol. AAPS PharmSciTech 2010;11:1034-44.
33. Malakar J, Sen SO, Nayak AK, Sen KK. Formulation, optimisation and evaluation of transpersonal gel for transdermal insulin delivery. Saudi Pharm J 2012;20:355-63.
34. Panda D, Si S, Swain S, Kanungo SK, Gupta R. Preparation and evaluation of gels from the gum of *Moringa oleifera*. Indian J Pharm Sci 2006;68:777-80.
35. Pathan IB, Setty CM. Chemical penetration enhancers for transdermal drug delivery systems. Trop J Pharm Res 2009;8:173-9.
36. Jain AK, Thomas NS, Panchangnula R. Transdermal drug delivery of imipramine hydrochloride. I. Effect of terpenes. J Controlled Release 2002;79:93-101.

How to cite this article

- M Saquib Hasnain, Poonam Rishishwar, Sadath Ali. Use of cashew bark exudate gum in the preparation of 4 % lidocaine HCL topical gels. Int J Pharm Pharm Sci 2017;9(8):146-150.