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Povidone iodine loaded film-forming topical gel and evaluation of its chemical stability

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ABSTRACT

The main aim of this study was to develop Povidone Iodine loaded film-forming gel for excellent wound healing property with various formulations, and corresponding application stratification was prepared with Povidone Iodine, polyethylene glycol-400, polyethylene glycol-4000, aloe vera, and honey. Povidone Iodine is a broad spectrum antiseptic for topical application in the treatment and prevention of infection in wounds. Among the antiseptic and antimicrobial substances, Povidone-Iodine still occupies its position of lasting importance in everyday human and veterinary medicine. Povidone-iodine products display the broadest spectrum of antimicrobial effect with high clinical efficacy together with extremely low toxicity in clinical practice. The purpose served by dressing includes protecting wounds, promoting healing, and providing, retaining, or removing moisture. Wound repairing is a complex process involving an integrated response by many different cell types and growth factors to achieve rapid restoration of skin integrity and protective function after injury. In recent years, there have been tremendous advances in the design and composition of bandages and dressings, and there are numerous wound care materials. The film-forming optimized gel formulation composed of povidone-iodine, polyethylene glycol-400, polyethylene glycol-4000, aloe vera, and honey and this composition provides suitable consistency, spreadability, and adhesiveness. The prepared trials were coded PGAH-01, PGAH-02, PGAH-03, PGAH-04, and PGAH-05, respectively. Among these all formulations, the PGAH-04 formulation parameters was found within the limit.

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INTRODUCTION

Wound recuperating is an organic process by which the structure and function of harmed skin are reestablished to their typical skin. For attractive injury care, the injury dressing plans must serve the following; (a) arrangement of dampness and impediment, (b) Security from contamination and diseases, and (c) simple application also, evacuation with the evasion of dressing-related injury (Singer and Dagum, 2008; Thu *et al.*, 2012). Germicides, as a preference for topical wound healing, will, in general, be germicidal and include a wide range

of antimicrobial movement than antibiotics (Leaper *et al.*, 2012a; Lachapelle *et al.*, 2013). Further-more, in contrast with nearly all antibiotics, antiseptics ease the chance of opposition developing owed to their different methods of activity, focusing on different parts of cell science in microbes (Lachapelle *et al.*, 2013). Therefore, the utilization of topical antiseptics agents ought to be disheartened if appropriate antiseptics are available (Bigliardi *et al.*, 2017). Besides, an ongoing WHO rule promotes the utilization of excellent antisepsis periople whereas reducing the use of general antibiotics (Bigliardi *et al.*, 2017; Chatterjee *et al.*, 2013). Many antiseptic are available for the deterrence and healing of infection sore care, and these includes iodine carriers (iodophores) with polyvinylpyrrolidone (or povidone) iodine, in addition to silver, Benzalkonium chloride, chlorhexidine, polihexanide, triclosan and octenidine and selected dyes such as Eosine. Among these povidone iodine include astonishingly fit for wound curing, together with its wide antimicrobial spectrum, efficacy against biofilms, lack of resistance, excellent permissibility, and its result on extreme inflammation. Owing to its fast, effective, wide-ranging antimicrobial properties, and good benefit report, povidone-iodine is anticipated to continue highly valuable healing for acute and chronic wounds in the near future (Chatterjee *et al.*, 2013). The pharmaceutical preparations of povidone-iodine are official in all pharmacopoeias and are alleged as efficient wide spectrum biocidal cause the *invitro* biocidal activity has been premeditated for era beside bacteria, moulds, yeast, viruses, protozoa, fungi, rickettsia, and actinomycetes. Aloe vera is a traditional indigenous medicative herb found throughout the Asian country. There are over 100 active biologic constituents found within aloe vera, which possesses astringent, antidiabetic, haemostatic, antiseptic, anti-inflammatory, anticancer, antidiarrhoeal, antiulcer, antibacterial, antioxidant and wound healing properties (El-Kased *et al.*, 2017). Honey is a nourishing thick carbohydrate-rich syrup, which was efficiently used since the ancient era in conventional medication. These days, honey is used due to its wide beneficial uses (Gulfraz *et al.*, 2011). It is a renowned antibacterial (Azim and Sajid, 2009), antiparasitic (Azim *et al.*, 2007), pain-reliever (Molan, 1999) and it has established competence against respiratory tract infections. Honey has the capacity to produce cytokine by stimulating human monocytes. The antibacterial activity of honey has also been revealed in vivo, with details of contaminated wounds dressed with honey becoming sterile in 3-6 days, (Branicki, 1981; Cavanagh *et al.*, 1970; Efem, 1993) 7 days (Efem, 1988; Phuapradit and Saropala, 1992; Armors, 1980) and 7-10 days (Mohamed *et al.*, 2018).

The aim of our present investigation is to evaluate the aloe vera and honey loaded film-forming povidone iodine topical gel and its chemical stability. The formulated batches have been characterized with regard to Physical description, pH, viscosity, spreadability, drug content, and drug release.

MATERIALS AND METHODS

Povidone Iodine be compassionately gifted from Drakt Pharmaceuticals, Vadodara, India. Honey was purchased from local Agriculturalists, India. Aloe vera was gifted by Hiran agroceuticals private limited, Madurai, India. Polyethylene glycol 400 and Polyethylene glycol 4000 were procured from SD Fine Chem. Ltd, Mumbai, India. All new substances and reagents used were of analytical status. The double-distilled water was filtered through a 0.45 μm membrane (cellulose acetate) before use.

Povidone Iodine Gel formulation

Five formulae of povidone-iodine loaded topical anhydrous gel was prepared by a conventional method (Indian Pharmacopoeia, 2018). Briefly, the anhydrous gel phase containing polyethylene glycol-400 and polyethylene glycol-4000 was heated up to 72°C±1°C and then cool the content under continuous stirring at 1500 rpm until to form a clear gel. Povidone Iodine was dissolved in polyethylene glycol-400, then add into the gel phase at 55°C±20°C under continuous stirring condition. Cool the content below 50°C and add aloe vera and honey in it slowly under continuous stirring until the gel was cooled to room temperature. The compositions of the formulated trial batch percentage (% w/w) and their codes is listed in Table 1.

Evaluation of povidone-iodine loaded topical anhydrous gel

Visual Inspection

The formulated povidone-iodine trials final gel were examined for their colour, consistency, homogeneity, texture (lumps) by visual check under a good light, viewed against a black and white background (Indian Pharmacopoeia, 2018).

pH determination

The pH was determined, 3.00 g each formulation were dispersed in 30.00 ml of purified water then measured by using a pH meter (pH Mettler-Toledo GmbH, Switzerland). The measurements of the pH of each formulation were replicated three times (Indian Pharmacopoeia, 2018).

Table 1: Formulae of povidone-iodine loaded topical anhydrous gel

Ingredients	Formulations (% w/w)				
	PGAH-01	PGAH-02	PGAH-03	PGAH-04	PGAH-05
Povidone Iodine *	5.00	5.00	5.00	5.00	5.00
Honey	2.00	3.00	3.00	3.00	2.00
Aloe vera	10.00	8.00	5.00	10.00	8.00
Polyethylene Glycol-4000	18.00	16.00	15.00	12.00	12.00
Polyethylene Glycol-400	Q.s	Q.s	Q.s	Q.s	Q.s

* 5.00 %w/w overage added in all five batches

Table 2: Evaluation of formulated povidone-iodine loaded anhydrous topical gel

Formulations	Parameters #				
	Appearance	pH	Viscosity (cPs)	Spreadability (gm cm/sec)	Drug Content (%w/w)
PGAH-01	Reddish Brown homogenous viscous gel	6.12	55,685.35	42.21	104.45
PGAH-02		5.65	42,720.08	39.60	104.93
PGAH-03		5.89	40,127.11	35.42	105.09
PGAH-04		5.49	35,005.41	28.34	105.17
PGAH-05		4.68	30,402.00	26.61	105.54

(n=3, ± SD)

Viscosity

The prepared Povidone-iodine Gel formulation viscosity was measured by using Brookfield Rotational Digital Viscometer DV II, model LVDV-E (in cPs). 500 g of prepared gel sample was loaded in the griffin standard beaker, and the T-bar spindle (S-96) was at 10 rpm, the temperature was maintained as 25±1°C (Indian Pharmacopoeia, 2018).

Spreadability

The spreadability of the povidone-iodine loaded topical anhydrous gel was resoluted by pressing 0.5 g gel between two horizontal plates (20 × 20 cm). After that, 5 g consistent weight was put on the upper plate and left for about 5 minutes, where no more distribution was expected. Diameters of spread circles were calculated in cm and were taken as relative values for spreadability. The results attained were the average of three values (Indian Pharmacopoeia, 2018).

Drug content

Assay of available Iodine

The content of Povidone-iodine in the prepared formulations, standard and sample were analyzed using the official Indian pharmacopoeia method (ICH QIA (R2), 2003).

Stability studies

The stability readings present the data of povidone-iodine topical gel value differ with time under diverse ecological features includes light, humidity, and temperature. The study was carried out based on the international conference on harmonization (ICH QIA (R2), 2003; Leaper *et al.*, 2012b). The studies were executed over a phase of 6months at 25°C±2°C/60%RH±5%RH (Long tenure), 30°C±2°C/65 % RH± 5%RH (transitional) and 40°C±2°C/75%RH±5%RH (Accelerated state). The samples were estimated at 0, 3 and 6 months for their pH, viscosity, spreadability and drug content, Besides samples, were visually observed for any physical instability (partition and aggregation)

RESULTS AND DISCUSSION

The role of iodine as an antimicrobial agent in wound care. For many centuries, povidone-iodine was used and tested in wound healing (Ripa *et al.*, 2002; Banwell, 2006). Like other antiseptics, in vitro, animal and clinical information with distinct concentrations and formulations are constantly collected in research of distinct models, evaluation criteria and quality, while some questions have not yet been answered (Banwell, 2006; Selvaggi *et al.*, 2003). The concentration formulation and temperature-dependent stability of povidone-iodine to free iodine serves to reduce safety and acceptability issues allied with skin contact to for-

Table 3: Stability study of Povidone loaded a topical anhydrous gel

Formulations	Conditions	Evaluation parameters *	Observations (Months)		
			0	3	6
PGAH-04	25°C±2°C/ 60%RH±5%RH	Appearance	Reddish brown smooth homogenous viscous gel	Reddish brown smooth homogenous viscous gel	Reddish brown smooth homogenous viscous gel
		pH	5.49	5.27	5.29
		Viscosity (cPs)	35.005.41	35.245.32	35.185.52
		Spreadability	28.34	27.43	28.50
		Drug content (%)	105.17	105.08	105.34
	30°C±2°C/ 65%RH±5%RH	Appearance	Reddish brown smooth homogenous viscous gel	Reddish brown smooth homogenous viscous gel	Reddish brown smooth homogenous viscous gel
		pH	5.49	5.31	5.46
		Viscosity (cPs)	35.005.41	35.524.78	38.789.11
		Spreadability	28.34	28.85	27.52
		Drug content (%)	105.17	105.02	104.98
	40°C±2°C/ 75%RH±5%RH	Appearance	Reddish brown smooth homogenous viscous gel	Reddish brown smooth homogenous viscous gel	Reddish brown smooth homogenous viscous gel
		pH	5.49	5.55	5.62
		Viscosity (cPs)	35.005.41	36.425.03	36.258.64
		Spreadability	28.34	28.01	26.25
		Drug content (%)	105.17	104.58	104.28

*(n=3±S.D.)

mer basic iodine formulations (Banwell, 2006) and emerge to defend against inhibition of granulation tissue formation. The in-vitro and in-vivo studies of higher concentration Povidone-iodine report shows, toxic to fibroblast. To rise above this problem, the concentration of Povidone Iodine was reduced, and the therapeutic activity was increased by the addition of honey and aloe vera (Indian Pharmacopoeia, 2018). The formulated povidone-iodine loaded anhydrous gel prepared with different inactive ingredients includes polyethylene glycol-400, polyethylene glycol-4000, aloe vera, and honey.

The formulated povidone-iodine loaded formulations were shown Reddish Brown homogenous viscous gel with a weak iodine flavor. The formulated batch PGAH-05, which has a low percentage of polyethylene Glycol-4000, aloe vera, and honey was shown slightly colour change in the appearance. In general, the pH of the gel is essential for evaluating the gel stability. Actually, pH alterations show the rate of chemical reactions that can offer an initiative on the quality of the final product. The pH of human skin normally ranges from 4.5 to 6.0. The developed formulations pH range was 4.68 to 6.12, which is near to neutral pH, non-fatty, and simply separable after the application. The rheology behavior and thixotropic properties can fill in as significant pointers for assessment of physical properties and the structural stability of the gel definition. The readied Povidone Iodine gel detailing consistency results between 20,000 cPs and 56,000 cPs. The gel consistency is stated to play an important part in its flow properties. The gel comprises of greater consistency the drug discharge from the gel is decreased. On the off chance that a similar gel has less consistency, the drug diffuses quickly into the dispersion medium. Thus, for the gel formulation, ideal consistency is important to get the most

extreme drug discharge. The prepared Povidone-iodine gel detailing thickness was found in the range 35,005.41 to 55,685.35 cPs. Higher consistency was accomplished by the addition of the high percentage of polyethylene glycol-4000. Spreadability and the drug of the prepared batches results were shown in Table 2. Among all formulations, PGAH-04 was selected as best formulation based on the physical and chemical parameters and the same was charged in stability study at diverse states includes, 25°C±2°C/60%RH±5%RH, 30°C±2°C/65%RH±5%RH and 40°C±2°C/75%RH±5%RH. During the stability study at the different condition the formulated gel appearance, pH, viscosity (cPs), spreadability and drug content (%)was checked at first, third and six months, and the results were depicted in the Table 3. Obtained results shown, there was no changes in their physical and chemical parameters as compared with the initial results.

CONCLUSIONS

The Povidone Iodine loaded film-forming topical gel with honey, and aloe vera was prepared by the conventional method, and the formulated gel physical and chemical characteristics was studied of its chemical stability. Five different formulations trials were prepared with various percentages of inactive ingredients to optimize the process and chemical stability of the Gel. Among these five trials, the PGAH-04 formulation result was found within the limit, and the physical appearance of the prepared gel texture was good.

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