WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

PREPARATION AND DEVELOPMENT OF IN-SITU HERBAL GEL FOR BURN INJURY TREATMENT

Dr. Viram Parmar[1], Solanki Vivek[2] , Kevadiya Dharmik[3] , Valiya Darshan[4] , Dhola Yash[5].

Department of Pharmacy , Principal, Gyanmanjari pharmacy college, Sidsar, Bhavnagar, Gujrat, India,
Department of Pharmacy ,Gyanmanjari pharmacy college, Sidsar road, Bhavnagar, Gujrat, India,
Department of Pharmacy , Gyanmanjari pharmacy college, Sidsar road , Bhavnagar, Gujrat, India,
Department of Pharmacy , Gyanmanjari pharmacy college, Sidsar road , Bhavnagar, Gujrat, India,
Department of Pharmacy , Gyanmanjari pharmacy college, Sidsar road , Bhavnagar, Gujrat, India.

ABSTRACT :

The skin is the largest organ of the human body and it's in direct contact with the environment. It can be damaged by heat, electricity, chemicals and most importantly, burning. Approximately 6-7 million peoples are suffer from skin burns every year in India. We aimed to create a Heat and pH sensitive herbal in-situ gel, which will form a gel in a part or area of the skin after being applied to the area or site of the burn. Development and evaluation of topical delivery systems to create in-situ gels for efficient use of antibiotics and burn healing. Aloe Vera, kiwi, broccoli and marigold are important herbs which are very use full in burn treatment and tissue remodeling and which is also contain antimicrobial, anti-inflammatory, analgesic with instant cooling instant cooling effect.Therefore, extracts of these plants are used as an active ingredient in the preparation of in-situ herbal gels for treatment of burns or wounds.

Keywords:- Burn injury, In-Situ gel , aloe vera ,kiwi, broccoli, marigold, carbopol 940, HPMC.

Introduction :

The burn injury was thermal injury cause by heat, electricity, radiation, acid, etc.[1'2] It refers to cell or tissue damage resulting from various factors such as inflammation, toxicity, and other microbial factors.[3'4] The burn injury was classified according to its depth and size. The burn effect on upper layer of epidermis is called first-degree burn, it's cause pain and red skin. The deep burn on epidermis layer cause pain and required surgery which is called as second-degree burn. A third-degree burn was deep to the dermis layer cause infection pain and required surgery and the fourth degree burn deeper to tissues, muscle, or bone they lead to loss of burn part.[5'6] Healing of skin burn will be completed in the two phases, first phase is proliferative phase and second was remodeling phase. The proliferative phase contains wound closing and revascularization by keratinocytes and fibroblasts. the remodeling phase contains wound maturation and scarring of wound by collagen fibers, elastin protein and fibroblast or myofibroblast.[7'8]

Now a days, the use of herbal products in the production of new drugs is increasing rapidly. Here from all the known and accessible plants such as aloe vera, kiwi, broccoli, and marigold are rich in many proteins and fibers, Like Keratin, elastin, collagen fibers, fibroblasts, etc.[9'10'11'12] which have wound healing, anti-bacterial, antioxidant, anti-inflammatory and tissue repairing property.[13'14'15'16] They also contain minerals, amino acid, vitamins, glucosinolates, lipids, lutein.[17'18'19]

1.Aloe vera

2. Actinidia diliciosa

3.Brassica oleracea.

4. Tagetes erecta

In recent years many types of drugs such as creams and gels have being prepared and are tested for the treatment of burns. However, this is difficult to use and utilize and cause illnesses during use. They cause harm or side effects, give pain, therefore need to improve other formulation for anti-inflammatory effect and burn healing. Such problems can be overcome by making in-situ gel formulations.

The development of in-situ gelling system was considerable in last few years. in-situ gelling system consists of the polymers which convert the solution in to gel after the change in physicochemical parameters, like temperature, pH, ion change.[20'21] In-situ gelling system is liquid at room temperature but

forms gel when it comes in contact with the body fluid or change of pH. [22'23] The pH triggered in-situ gel is therapeutically stable, non-irritant and provide sustained release of drug.[24] They can be easily applied in liquid form to site to drug absorption and assist in enhansing the bioavability of drug.[24] In the formulation of in-situ gel Carbopol 940 and hydroxypropyl methycellulose (HPMC) was used.[25]

Materials and methods :

- **Materials**

Aloe vera and *Actinidia deliciosa* were collected from the local farm and the *Brassica oleracea* and *Tagetes erecta L.* ware purchased from the market. deionized water was obtained from royal chemicals. carbopol 940 and HPMC was purchased from royal chemicals Bhavnagar, India.

- **Preparation of the Extract**

Aloe vera gel, *Actinidia deliciosa*, *Brassica oleracea* and *Tagetes erecta L.* were used for extraction. extracts were obtained by decoction and distillation process using distillation unit.[26'27'28] all the extraction process was completed by using deionized water.

- **In-site gel preparation**

To prepare the gel, the desired concentration of Carbopol 940 and HPMC were dissolved in water at 80 °C with constant stirring for half an hour and placed for 24 hours.[29'30] Once it dissolves, add the extract with constantly stirring and prepared different formulations of gel.

Tabel No.1 composition of formations

Formulations	F 1	F 2	F 3	F4	F 5	F 6	F 7	F 8	F 9
Carbopol 940	0.05% conc.	0.07% conc.	0.09% conc.	0.1% conc.	0.15% conc.	0.18% conc.	0.2% conc.	0.25% conc.	0.3% conc.
HPMC	0.2% conc.	0.25% conc.	0.3% conc.	0.4% conc.	0.55% conc.	0.65% conc.	0.8% conc.	0.95% conc.	1% conc.
Aloe vera	20 ml	20 ml	16 ml	20 ml	20 ml	18 ml	20 ml	28 ml	20 ml
Kiwi	10 ml	9 ml	11 ml	9 ml	9 ml	10 ml	9 ml	10 ml	10 ml
Broccoli	8 ml	7 ml	9 ml	15 ml	8 ml	9 ml	10 ml	9 ml	8 ml
Merigold	12 ml	14 ml	14 ml	6 ml	13 ml	13 ml	11 ml	13 ml	12 ml

*All formulation are for up to 100 ml

In-site gelling system evaluation :

- **Physical parameters**

The in-situ gel preparation was tested for appearance, transparency, viscosity, temperature of gelling, pH and gelling time, etc.

- **Measurement of pH**

The pH value was measured by using a digital pH meter. The pH meter was calibrated using buffer solutions of pH 4 and pH 7. The required quantity of gel was taken in beaker and the pH was measured by using pH meter.[31]

- **Appearance**

The appearance of formulations was evaluated by clarity. The clarity of the formulation was evaluated and measure by visual method against the white and dark background.[31]

- **Gelling time**

The gelling time of prepared formulations was evaluated by time taken for transmission of liquid phase to gel. The time taken for gel formulation was determined by test tube inversion method. The pH 7 buffer solution was transferred to test tube and placed in water bath and the prepared formulations were added into the test tube at 36°C to 40°C.[31]

- **Gelation Temperature**

The formulation's gelation temperature was measured by heating the formulations in water bath and observed the viscosity of formations.[32]

- **Rheological studies**

The formulation's viscosity was measured by using digital viscometer (Brookfield). The viscosity of the prepared formulations was evaluated at different pH and temperature. The viscosity was increased when change in pH and temperature.[33]

- **Antibacterial activity**

The antibacterial activity of the formulation was evaluated by the agar diffusion test by using a cup plate technique. The 100 ml of nutrient agar media was prepared and sterilized in an autoclave for 1 hr. The microorganism solution was poured into the medium. This was done in aseptic condition.20 ml of the agar solution was poured into each Petri plate. After the solution solidification, the prepared formulation's were poured into the cup of sterile nutrient agar Petri plate. After the diffusion, the plates were incubated at 37°C for 24 hrs. The zone of inhibition was measured around each cup and compared with the control. The process was done in a laminar airflow unit.

Result's and discussion :

- **Appearance of formulations**

The prepared formations were shown clear appearance against the white and dark background.

- **Viscosity measurement**

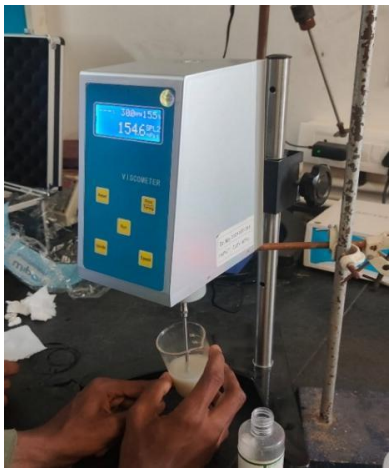
The viscosity of the prepared formations was evaluated by using the digital viscometer by using spindle no.2 at 30 RPM. The formations viscosity was measured at different pH and temperature. The formulation was stable at pH 6 to 6.4 and at room temperature. They form gel when pH changes to 7.2 to 7.6 and when temperature increases to 36 ℃ to 40 ℃.

- **pH determination**

The pH value of the formulation was evaluated by using a digital pH meter . The pH meter was calibrated using pH 4 and pH 7 buffer solutions. The pH range of the formulation is 5.8-6.4 . The viscosity of the formulation increases with increasing pH. The prepared formations viscosity at different pH values was measured using NaOH solution. The formulations evaluation was shown in Table 2.

Table no . 2

Formulations	Clarity	pH	Viscosity	pH	Viscosity	Temperature
F 1	Clear appearance	6.4	13.2 mPa•S	7.8	76.9 mPa•S	40℃
F 4	Clear appearance	6.1	15.7 mPa•S	7.1	110.9 mPa•S	39℃
F 7	Clear appearance	5.9	25.5 mPa•S	6.8	154.6 mPa•S	35℃



- **Gelling time**

The prepared formulation' s gelling time was evaluated by test tube inversion method. the prepared formulations were transferred to gel within a 7 to 8 seconds.

- **Gelling temperature**

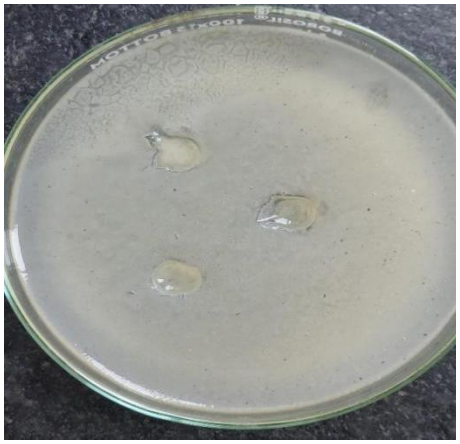
The prepared formations were stable at room temperature. the viscosity of the formation was increases with the temperature increases. the formations were forming gel at the temperature range of 36 ℃ to 40℃. The viscosity of the formations ware evaluated at different temperatures shown in table no 3.

Table no. 3

Formulations	Temperature	Viscosity
F 1	40℃	95.6 mPa•S
F 4	39 ℃	115 mPa•S
F 7	35 ℃	130.6 mPa•S

- **Antibacterial activity**

The antibacterial evaluation study was performed for different prepared formulation's using Escherichia coli bacteria. The formulation F4 was given best activity compare to others. The zone of inhibition of formulation F4 was found to be 19 mm to 23 mm. The evaluation study indicated formulation retains its antibacterial activity when formulated as a gel forming topical drug delivery dosage form system against the bacteria.



Comparison

F4 : Zone of inhibition

Conclusion :

The prepared formulation is use in the treatment of burn's. It was successfully formulated as pH-sensitive in-situ herbal gel by carbopol 940 and HPMC as a gelling agent with aloe vera, kiwi, merigold and broccoli herb's. The appearance, pH, temperature, viscosity and antimicrobial activity of formulation were found to be satisfactory. When the change of pH the formulation F7 contains higher viscosity compare to F1 and F4. The formulation F4 evaluation of appearance, pH, viscosity, gelling time and antibacterial activity was given the best results. That was used for ideal preparation of burn healing in-situ gel. Also it retains antibacterial activity when it is transformed in to gel against bacteria.

REFERENCES :

1. Jeschke, M.G., van Baar, M.E., Choudhry, M.A. et al. Burn injury. Nat Rev Dis Primers 6, 11 (2020). https://doi.org/10.1038/s41572-020-0145-5
2. Shpichka, A., Butnaru, D., Bezrukov, E.A. et al. Skin tissue regeneration for burn injury. Stem Cell Res Ther 10, 94 (2019). https://doi.org/10.1186/s13287-019-1203-3
3. Jeschke, M.G., Rehou, S., McCann, M.R. et al. Allogeneic mesenchymal stem cells for treatment of severe burn injury. Stem Cell Res Ther 10, 337 (2019). https://doi.org/10.1186/s13287-019-1465-9
4. Shakespeare P. Burn wound healing and skin substitutes. Burns. 2001 Aug;27(5):517-22. PMID: 11451610.
5. Atiyeh BS, Gunn SW, Hayek SN. State of the art in burn treatment. World J Surg. 2005 Feb;29(2):131-48. Doi: 10.1007/s00268-004-1082-2. PMID: 15654666.
6. Ja, Garcia-Espinoza & Vb, Aguilar-Aragon & Eh, Ortiz-Villalobos & García-Manzano, Roberto & Barker Antonio, Alan & Aron, Jaime & García-Espinoza, Jaime. (2020). Burns: Definition, Classification, Pathophysiology and Initial Approach. International Journal of General Medicine. Volume 5. 2327-5146. 10.4172/2327-5146.1000298.
7. Rowan MP, Cancio LC, Elster EA, Burmeister DM, Rose LF, Natesan S, Chan RK, Christy RJ, Chung KK. Burn wound healing and treatment: review and advancements. Crit Care. 2015 Jun 12;19:243. Doi: 10.1186/s13054-015-0961-2. PMID: 26067660; PMCID: PMC4464872.
8. Nielson CB, Duethman NC, Howard JM, Moncure M, Wood JG. Burns: Pathophysiology of Systemic Complications and Current Management. J Burn Care Res. 2017 Jan/Feb;38(1):e469-e481. Doi: 10.1097/BCR.0000000000000355. PMID: 27183443; PMCID: PMC5214064.

9. Hekmatpou D, Mehrabi F, Rahzani K, Aminiyan A. The Effect of Aloe Vera Clinical Trials on Prevention and Healing of Skin Wound: A Systematic Review. Iran J Med Sci. 2019 Jan;44(1):1-9. PMID: 30666070; PMCID: PMC6330525.
10. Mohajeri G, Masoudpour H, Heidarpour M, Khademi EF, Ghafghazi S, Adibi S, Akbari M. The effect of dressing with fresh kiwifruit on burn wound healing. Surgery. 2010 Nov;148(5):963-8. Doi: 10.1016/j.surg.2010.02.013. Epub 2010 Apr 8. PMID: 20381106.
11. Ares AM, Nozal MJ, Bernal J. Extraction, chemical characterization and biological activity determination of broccoli health promoting compounds. J Chromatogr A. 2013 Oct 25;1313:78-95. Doi: 10.1016/j.chroma.2013.07.051. Epub 2013 Jul 16. PMID: 23899380.
12. Rahman MT, Hasan M, Hossain MT, Islam MS, Rahman MA, Alam MR, Juyena NS. Differential efficacies of marigold leaves and turmeric paste on the healing of the incised wound in sheep. J Adv Vet Anim Res. 2020 Dec 5;7(4):750-757. Doi: 10.5455/javar.2020.g477. PMID: 33409322; PMCID: PMC7774798.
13. X, Munoz. (2015). Extraction, Characterization and Properties of the Gel of Aloe Vera (Aloe barbadensis Miller) Cultivated in Chile. Medicinal & Aromatic Plants. 04. 10.4172/2167-0412.1000199.
14. Mohajeri G, Safaee M, Sanei MH. Effects of Topical Kiwifruit on Healing of Chronic Bedsore. Indian J Surg. 2015 Dec;77(Suppl 2):442-6. Doi: 10.1007/s12262-013-0869-5. Epub 2013 Jan 31. PMID: 26730042; PMCID: PMC4692920.
15. Nicolas-Espinosa J, Yepes-Molina L, Carvajal M. Bioactive peptides from broccoli stems strongly enhance regenerative keratinocytes by stimulating controlled proliferation. Pharm Biol. 2022 Dec;60(1):235-246. Doi: 10.1080/13880209.2021.2009522. PMID: 35086428; PMCID: PMC8797740.
16. Soraya Razai ,kobra Rahzani , Davoud Hekmatpou and Alireza Rostamu. Effect of oral calendula officinalis on second-degree burn wound healing. Volume 9:-1-7 Doi: 10.1177/20595131221134053.
17. Pj nivethaa and G. Sithdharth. Aloe vera – processing and Gel extraction techniques volume.1 issue -10, June 2021, Article 47.
18. Oliviero T, Lamers S, Capuano E, Dekker M, Verkerk R. Bioavailability of Isothiocyanates From Broccoli Sprouts in Protein, Lipid, and Fiber Gels. Mol Nutr Food Res. 2018 Sep;62(18):e1700837. Doi: 10.1002/mnfr.201700837. Epub 2018 Apr 14. PMID: 29532635; PMCID: PMC6174964.
19. Sowbhagya HB, Sushma SB, Rastogi NK, Naidu MM. Effect of pretreatments on extraction of pigment from marigold flower. J Food Sci Technol. 2013 Feb;50(1):122-8. Doi:10.1007/s13197-011-0313-4. Epub 2011 Feb 20. PMID: 24425896; PMCID: PMC3550940.4.
20. Kolawole OM, Cook MT. in-situ gelling drug delivery systems for topical drug delivery. Eur J Pharm Biopharm. 2023 Mar;184:36-49. Doi: 10.1016/j.ejpb.2023.01.007. Epub 2023 Jan 13. PMID: 36642283.
21. Dhalkar, Priyanka & Jagtap, Shivani & Jadhav, Suraj & Redkar, Mayuresh & Karande, Biradev. (2019). Formulation and Evaluation of in-situ Gel Model Naproxen. Asian Journal of Pharmacy and Technology. 9. 204. 10.5958/2231-5713.2019.00034.5.
22. Neha Bisht, Lakshman Goswami, preeti Kothiyal. Preparation and evaluation of in-situ oral topical gel of levofloxacin by using combination of polymers. Indian journal of drugs, 2014,2(4), 142-151.
23. .Dattatraya j. Yadav , Harish k. Kunjwani, Sarika s. Suryawanshi. Formulation and evaluation of thermosensitive IN-situ gel of salbutamol sulphate for nasal drug delivery system. International journal of pharmacy and pharmaceutical sciences, Vol 4 ,suppl 4 2012.
24. K.S. Rathore, in-situ gelling ophthalmic drug delivery system. International journal of pharmacy and pharmaceutical sciences Vol 2 , suppl 4 , 2010
25. Jike Song a, Hongsheng Bi b, Xiaofeng Xie b, Junguo Guo c, Xingrong Wang b, Damei Liu a, Preparation and evaluation of sinomenine hydrochloride in-situ gel for uveitis treatment, International Immunopharmacology, Volume 17, Issue 1, September 2013, Pages 99-107
26. Munoz OM , leal , quitral v and cardemil L (2015). Extraction, Characterization and Properties of the Gel of Aloe Vera (Aloe barbadensis Miller) Cultivated in Chile. Medicinal & Aromatic Plants. 04. 10.4172/2167-0412.1000199.
27. Martyna Natalia Wieczorek,Małgorzata Majcher and Henryk Jeleń, comparison of three extraction techniques for the determination of volatile flavor components in broccoli. MDPI .https://doi.org/10.3390/foods9040398
28. Khulood M. Alsaraf . Extraction and clinical application of calendula officinalis l. Flowers cream. IOP conference series: material science and engineering. DOI 10.1088/1757-899X/571/1/012082
29. Garala K, Joshi P, Shah M, Ramkishan A, Patel J. Formulation and evaluation of periodontal in-situ gel. Int J Pharm Investig. 2013 Jan;3(1):29-41. Doi: 10.4103/2230-973X.108961. PMID: 23799203; PMCID: PMC3687234.
30. 30.Marcela Miranda, Xiuxiu Sun, Anna Marín, Luana Cristina dos Santos, Anne Plotto, Jinhe Bai, Odílio Benedito Garrido Assis, Marcos David Ferreira, Elizabeth Baldwin, https://doi.org/10.1016/j.fochx.2022.100249
31. Praveen D. Chaudhary, Ujwala S. Desai. Formulation and evaluation of niosomal in-situ gel of prednisolone sodium phosphate for ocular drug delivery. International journal of applied pharmaceutics Vol 11, Issue 2, 2019.
32. Patel P, Patel P. Formulation and evaluation of clindamycin HCL in-situ gel for vaginal application. Int J Pharm Investig. 2015 Jan-Mar;5(1):50-6. Doi: 10.4103/2230-973X.147233. PMID: 25599033; PMCID: PMC4286835.
33. Mandal S, Thimmasetty MK, Prabhushankar G, Geetha M. Formulation and evaluation of an in-situ gel-forming ophthalmic formulation of moxifloxacin hydrochloride. Int J Pharm Investig. 2012 Apr;2(2):78-82. Doi: 10.4103/2230-973X.100042. PMID: 23119236; PMCID: PMC3482769.