ISSN: 2322 - 0902 (P)
ISSN: 2322 - 0910 (O)

International Journal of Ayurveda and Pharma Research

Review Article

A CRITICAL REVIEW ON THERMO-SENSITIVE VAGINAL GEL FOR THE FOUNDATION OF PREPARING THERMO-SENSITIVE VAGINAL GEL OF PVK (*PANCHVALKAL KASHAYA*) EXTRACT

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Article info

Article History:
Received: 22-01-2022
Revised: 22-02-2022
Accepted: 05-03-2022

KEYWORDS:
Panchvalkal Kashaya, Thermosensitive, Vaginal, Gel, STD, Ayurvedic, Formulation, HIV/ AID, Vaginal candidiasis.

ABSTRACT

RTI (Reproductive Tract Infection) is the vital cause of suffering in women and neonates. According to WHO estimation 340 million new cases of curable STI (Sexually Transmitted Disease) other than HIV/AIDS occurs every year, most of which are occurring in developing countries. Genital tract infection is the prime cause of most gynaecological disease. Vaginal candidiasis is the most common cause of Genital tract infection. It (Vaginal candidiasis) is a common condition and up to 75% of all women suffer at least one episode of this infection during their life time. For treating the pathological condition of genital tract, direct application or self application of medicine is very difficult and the residence time of the medicine is less due to self cleansing properties of vaginal canal. Application of the drug in other route may cause systemic adverse reaction. To overcome this arduous situation, in situ thermo-sensitive gel form has great importance. In this article an attempt have been made for the review of the thermo-sensitive vaginal gel and the scholar has gathered the basic knowledge to develop an Ayurvedic formulation *Panchavalkal kashaya* thermo-sensitive vaginal gel by this review. This work will be done in School of Pharmaceutical Science, Shoolini University, Solan, HP.

INTRODUCTION

The needs to develop new dosages form are to increase patient's compliance, effective therapeutic activities in small quantity, increase the contact time in the target surface, maintain a constant plasma level by sustain release and also increase the bioavailability of the drug.[1] Thermo-sensitive in situ gel is a new drug delivery system, when applied it will undergo phase change to gel due to condition of PH, electrolytes and temperature. In situ forming system are liquid aqueous solution before administration, but convert to gel under physiological condition.[2] There are several possible mechanisms that lead to in situ gel formation like solvent exchange, UV irradiation, ionic cross linkage, PH change and temperature modulation.[3] RTI (Reproductive Tract Infection) is the vital cause of suffering in women and neonates.

Access this article online

Quick Response Code

https://doi.org/10.47070/ijapr.v10i3.2223

According to WHO estimation 340 million of new cases of curable STD (Sexually Transmitted Disease) other than HIV/AIDS occurs each year, most of which are occurring in developing countries.[4] Genital tract infection is the prime cause of most gynaecological diseases. Vaginal candidiasis is the most common cause of Genital tract infection. It is a common condition and up to 75% of all women suffer at least one episode of this infection during their life time.[5] The pathological condition occurs due to Genital tract infection always treated with conventional drug delivery systems like creams, gels, tablets, foams, pessaries and irrigations.[6] Due to less residence time of the drug in genito- urinary tract, the efficacy of all of these treatments are limited. The less residence time of drug is because of self cleansing action of vaginal tract. Due to this conventional vaginal delivery systems are susceptible to wash out quickly. (Deshpande et al, 1992, Wolfsson, 2002).[7] Usually the protective mechanism of the genitourinary tract, reduces the residence time of the drug in the infective surface and due to this impairing therapeutic efficacy of the drug. To overcome this arduous situation multiple and frequent administrations of the drug was

necessary for the treatment. The most important confront in vaginal drug delivery is patient tolerance when administering the dosages forms and following the repeated dose therapeutic procedure. The vaginal pathological treatment can be notably improved if a delivery system can retain the drug at the site of administration for a prolong period compared to conventional dosages form.[8] Thermo-sensitive vaginal gel is the vaginal drug delivery system, which prolong the duration of persistence of drug in vagina. Some reviews of research studies of Thermo-sensitive gel have given below for the better understanding of the procedure of preparation and analytical parameters. By which anyone can adopt a suitable method according to the need.

MATERIALS AND METHODS

Amphotericin B (AmB) is a very effective antifungal medicine used in serious fungal infection in human. But the drawbacks of this medicine are its renal toxicity and low water solubility (Recher et al, 2000).[9] To conquer this problem, several carrier systems like liposomes, colloidal dispersions, microspheres and micelles have been developed. In this study, Amphotericin was mixed with cyclodextrins (cyclic oligosaccharide) to form inclusion complexes with drug molecules to increase their aqueous solubility, to reduce side effects and with novel polymer pluronic based multi block copolymers (MBCP-2). MBCP-2 was a temperature- sensitive polymer that would degrade under locally acidic physiological conditions for the preparation of thermo-sensitive muco adhesive vaginal gel. It was prepared according to cold method. The phase solubility study was performed. This study showed that HPγCD (hydroxypropyl-γ-cyclodextrin) improved the aqueous solubility of AmB proportionally the concentration of HPγCD.

Thermal transition studies showed that the aqueous solution of the polymer gelled at body temperature and that the gelation temperature of the polymer solution was dependant on polymer concentration.

The gel in the pH 5.0 was completely eroded in 4 days, where as the gel in the pH 7.4 and 9.0 eroded in around 6 weeks.

In vitro study the AmB-HPγCD complx-loaded gel showed a prolonged release in pH 7.4 and pH 9.0. But in case of pH 5.0, the constant release of the drug takes place, which was completed within 3 days. It was reported previously that the rate of dissolution of pluronic gel is actually the controlling factor in drug release (Bilensoy et al 2006). In cyto toxicity assay study, it showed that the cell viability of AmB-HPγCD complex loaded gels were higher than free AmB. So this is proved that HPγCD and MBCP-2 reduced the cyto toxicity.[10]

Fungal infection of Genital tract is the most frequent gynaecological diseases. Imidazole derivative antifungal agent such as clotrimazole is commonly used as antifungal drug for the treatment of Genital tract infection. It is a locally active drug and it has no major side effect. In this experiment the study was done to develop muco adhesive, thermo-sensitive vaginal gel for clotrimazole, B- cyclodextrin complex. This gel was prepared using clotrimazole (1%), thermo-sensitive polymer pluronic F 127 (20%) with mucoadhesive polymer such as carbopol 934 (0.2%) and hydroxypropyl methyl cellulose (0.2%). Clotrimazole was dissolved with 1:1 molar ratio in B-cyclodextrin to increase the aqueous solubility of the formulation. The inclusion complex formed by the clotrimazole and B-cyclodextrin inclusion was studied by using various techniques, like H NMR Spectroscopy, FTIR Spectrometry, Differential Scanning Calorimetry, Scanning Electron Microscopy, phase solubility study and determination of stability constant. The measurement of gelation temperature and rheological behaviour of different formulations at varying temperatures were evaluated. In pH 5.5 citrate buffer in-vitro drug release character of the gels were determined. In the result it was shown that complex with cyclodextrin slowed down the release of clotrimazole considerably. Carbopol 934 was found to interact with B-cyclodextrin, inducing precipitation. When we consider the rheological properties, thermo-sensitive in situ geling was obtained with formulation containing drug: cyclodextrin complex rather than with free drug. So the formulation was formed in this experiment showed the thermo- sensitive and mucoadhesive properties containing clotrimazole: B-cyclodextrin 1% with 0.2% hydroxyl propyl methyl cellulose in pluronic F 127 (20%) gel providing continuous and prolonged release of active material above MIC value.[11]

In this research the in situ gel formulation was developed using the drug Tinidazole (TNZ) which can give effective treatment over the BV (Bacterial Vaginosis). For the development of thermo-sensitive vaginal gel the scholar had used Tinidazole (TNZ) Polaxomer 407 (Thermo-sensitive polymer) and MPMC E100 or Carbopol 941 NF (Mucoadhesive polymer). Two formulations were developed using the mucoadhesive polymer MPMCE100 and Carbopol. Optimized on the basis of various evaluation parameters, Gelation temperature (Tgel) and pH of two batches were found in range of 36.6 to 38.6°C and 4.20 to 5.03. Viscosity was found in range of 1100-2050cps at 25°C and 4800-6530cps at 37°C. Spreadability was found in range 16-20cm. Mucoadhesive properties, antimicrobial study, in vitro drug release, vaginal irritation study of these two formulations were perfectly done.

The result of the texture characterization of formulation formed by 20% Polaxamer and 0.5% HPMC E 100 showed better mechanical properties, good mucoadhesive strength and it gives sustained drug release for 7 hours.[12]

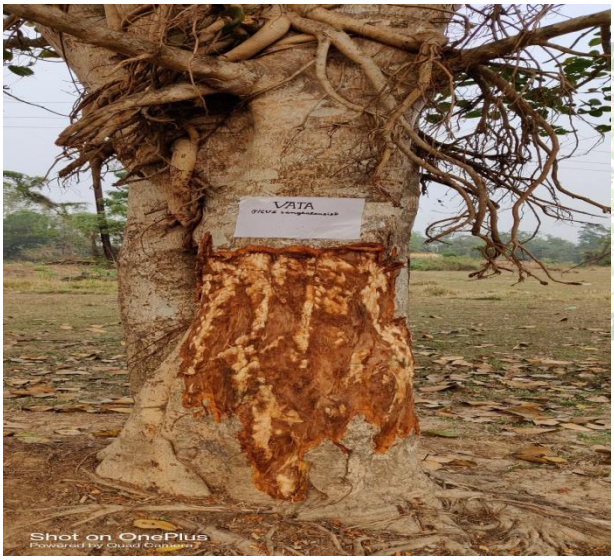
Muconazole nitrate ($C_{18}H_{14}Cl_4N_2O$) is a drug which is used for fungal infection. But it is hydrophobic in nature. So it has low aqueous solubility. Due to this properties it produces a negative impact on antifungal efficacy, causes more side effects. Pharmacokinetic variability is occurred due to hydrophobic nature. Finally drug resistance is developed. To get over this arduous situation in this experiment 9 formulations of thermo-sensitive mucoadhesive muconazole nitrate gel were developed using different muco adhesive polymers like Hydroxypropyl methyl cellulose (HPMC), S-carboxymethyl Cystine (SCMC), Carbopol, Polycarbophil in different concentration for the treatment of vaginal candidiasis. The thermo-sensitive gel was developed using the thermo-sensitive polymer Pluronic F127 along with bioadhesive polymers such as carbopol 934, HPMC, SCMC and polycarbophil with cold method. By using FTIR (Fourier Transform Infrared Spectroscopy) drug polymer compatibility study was done. The evaluation of gelation temperature, gelation time, viscosity, bioadhesive strength and drug release were done for the prepared formulations. The formulations which formed by the combination of pluronic F-127, polycarbophil, carbopol-934 showed optimum gelation temperature, gelation time, viscosity, bioadhesive strength with sustained release for 12 hours. However in stability study, it showed insignificant change in physical properties and drug content at 25°C/60% RH for 3 months.[13]

Metronidazole is considered a drug of choice for the treatment of bacterial vaginosis for prolong periods. The oral intake of metronidazole for prolong period causes various systemic disturbances and raises the potential toxicity. So in this study to overcome these problems, local vaginal application of in situ metronidazole thermo-sensitive gel was developed. 8 formulations were developed in this experiment. Unlike other studies, here the mucoadhesive polymers were not used. In place of mucoadhesive polymer, two thermo-sensitive polymers were used; Pluronic F-127 (PF- 127) and Pluronic F-68 (PF-68). The second polymer PF-68 was used for mucoadhesion. With PF-127 alone four formulations (F_1, F_2, F_3, F_4) were developed and another 4 formulations (F_5, F_6, F_7, F_8) with the combination of PF-127 and PF-68. When the formulations were developed their analytical parameters were checked like gelation temperature (T_{gel}), in vitro drug release, rheological properties, mucoadhesion properties and vaginal tolerability study. The gelation temperature decreased with increasing PF-127 concentration. The T_{gel} temperature was regulated within the acceptable range like 25°C-37°C by addition of PF-68. It was seen that when the Pluronic concentration increased the in vitro drug release decreased, viscosity and mucoadhesive force increased. Histo-pathological examination of rabbit vagina showed normal histology.[14]

In the imidazole group of antifungal drug Fluconazole is the high efficacy and safer drug than other drugs of this group. In this experiment the polymer Polaxamer 407 was used as thermo-sensitive polymer to prepare a thermo-sensitive vaginal gel. For the purpose of mucoadhesion, polymer Hydroxyethyl cellulose (HEC), Hydroxy propyl methyl cellulose (HPMC), Carbopol-974 (C-974) and Polycarbophil were used. 10 formulations were developed using cold method. 6 formulations were developed along with P-407 increasing the % of polymer and 4 with different mucuadhesive polymers. These formulations were evaluated for appearance, clarity, pH, gelling ability, gelling time, gelling temperature, viscosity, spreading time, ex vivo mucoadhesion, in vitro dissolution, morphological characteristic by SEM and in vitro antifungal efficacy against *Candida albicans*, in vivo irritation test was assessed in Newzealand female rabbit. It was shown that the formulation prepared using 18% w/w P-407 with 0.4% HEC was found to be clear, transparent, forming a quick and stable gel with shear thinning behaviour and excellent mucoadhesion. If the formulation dissolved with 5.2 pH citrate buffer released 72.21% FCZ in 8 hours and showed stronger antifungal activity as compared to the marketed formulations. In vivo irritation test, it showed no irritation after 10 days of exposure of the formulation.[15]

Inspite of considerable benefits of described thermo- sensitive vaginal gel, there are chances of drug resistance towards microbes due to its continuous and long term use. The most important hindrance of this preparation is its serious side effect to hypersensitive persons. Due to these above mentioned disadvantages the universal acceptance of Ayurvedic medicine is increasing day by day. The advantage of natural drugs is its way of acting in natural way according to the human physiology and pathology. To overcome these unwanted hazards of chemical pharmaceutical products, an attempt will be made to prepare a natural thermo-sensitive gel "*Panchavalkal Kashaya* thermosensitive vaginal gel" from *Panchavalkal* extract for the treatment of uncomplicated leucorrhoea. In most of the basic Ayurvedic text combination of different drugs (natural drug) were described for the treatment of different diseases. The intention of the combination is to increase the potency of the drugs. *Panchavalkal* is the most common example of the combination groups. It is the combination of the barks

of the five plants like *Vata* (*Ficus bengalensis* Linn), *Udumbara* (*Ficus racemosa,* Linn), *Peepal* (*Ficus religiosa,* Linn), *Plaksha* (*Ficus infectoria/Ficus lacer*) and *Shirish* (*Albizzia lebbeck* L), in equal proportions. The most relevant Ayurvedic text like *Charak Samhita, Sarangdhara Samhita, Kasyapa Samhita, Bharat bhashaijya Ratnakar* and *Bhavaprakasha* were described this combination (*Panchavalkal*) for the treatment of *Sthree roga* (gynaecological disease), wound and ulcers. V-gel and Petaphyte-5 cream are the two Ayurvedic products based on *Panchvalkal* which are available in market. So many studies on *Panchavalkal Kashaya* have done by the scholars in different institution. But the written documents are not available unfortunately. Viridis Biopharma Pvt Ltd also developed a cream from *Panchvalkal* for burn and episiotomy wound. From *Samhita* period*, Panchavalkal Kashaya* had proved as a strongest combination for its antifungal, antibacterial activities. In 2013, CCRAS developed a vaginal cream from the extract of modified PVK (*Panchavalkal Kashaya*). The cream was prepared with 0.4%w/w of hydro alcoholic extract of each plant, Carbopol 940, a polymer 0.58%, Propylene Glycol 7.0% and purified water quantity sufficient. Preclinical study for vaginal tolerability in rabbits and dermal tolerability had done successfully. Clinical study also carried out. In clinical study >95% showed cure or partial relief of the symptoms[16]. But by the application of cream in the vaginal canal, the physiological conditions imposed by the protective mechanisms of the vagina washed out the cream and the residence time of the cream in the vaginal canal will be reduced. To achieve the therapeutic efficacy of the medicament, frequent application of the medicine will be required. To overcome this problem there is an imperatively need of formulation (Ayurvedic) whose residence time is more in the target surface to increase the contact time by which the therapeutic efficacy will be achieved. This requirement is fulfilled by thermo-sensitive vaginal gel due to gel forming quality at body temperature. So in future, the scholar will develop the thermo- sensitive vaginal gel with PVK extract.

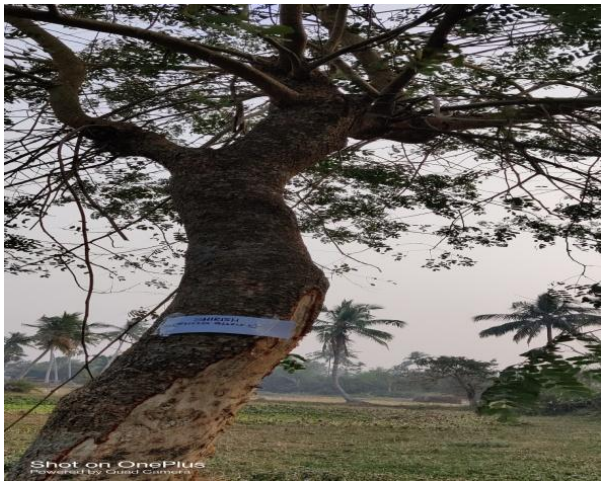


***Vata* (*Ficus bengalensis* Linn)**

***Peepal* (*Ficus religiosa* Linn)**

***Udumbara* (*Ficus racemosa* Linn)**

***Plaksha* (*Ficus infectoria/Ficus lacer*)**



***Shirish* (*Albizzia lebbeck* L)**

The method used for separate the medicinally active portion of the plant tissues is extraction. In this procedure extract will collect from the plant parts by using selective solvant medium through standard procedure. In future at the time of extraction of *Panchavalkal* the scholar will like to select the hot continuous extraction (Soxhlet) method. For the preparation of thermo-sensitive vaginal gel of PVK extract the scholar will collect the crude drugs. Then clean and dry it properly. After that the scholar will cut the drugs into small pieces. Then grind it in a pulverizer. This dry powder will be collected and extraction will be done by soxhet method. Then the extract will mix with Cyclodextrin to increase its aqueous solubility.

Every polymer have high molecular weight and are widely used in pharmaceutical systems as suspending, adjuvants, adhesives, imulsifying agents and coating material for controlled and site specific drug delivery system. Polaxamers are the most suitable co-polymers for the preparation of Tgel because of its amphiphilic characters. In future the scholar may use this polymer for preparing *Panchavalkal Kashaya* thermo-sensitive vaginal gel due to this advantase of the polymer. Owing to weak mechanical strength of Poloxamer, it causes rapid erosion in vaginal canal. To overcome these difficulties and increase the contact time in the vaginal surface, it will mix with the gel with mucoadhesive carbopol (C-974 or C-980). The thermo-sensitive vaginal gel will be prepared with the addition of polymer Poloxamer, Carbopols and PVK extract with Cyclodextrin inclusion. After preparation of the respective gel the process will be discussed. The above process are the hypothesis for the preparation of the "*Panchavalkal Kashaya* thermosensitive vaginal gel".

DISCUSSION

If we mix the drug with Cyclodextrin (cyclic oligosaccharide) which make inclusion, that increase the aqueous solubility.[17]

Cyclodextrins are cyclic oligosaccharides, formed by α-1, 4- linked glucose unit with a hydrophilic outer surface and a lipophilic central cavity. The action of Cyclodextrin is it takes the drug molecules into the central lipophilic cavity. By this action the physical and chemical properties of the drug will be changed. Drug/CD inclusion can increase the aqueous solubility, physical and chemical stability and improvement in drug delivery through biological membranes.[18]

Self assembling block polymers like Poloxamer, PEG (Poly Ethylene Glycol)/PLA (a biodegradable thermoplastic derived from lactic acid), PEG/PLGA (copolymer of polylactic acid (PLA) and poly glycolic acid (PGA) are diblock, triblock and multiblock polymers. So they contain two, three or more monomeric units of different solubility. Thus in solution and at low concentration, these amphiphilic molecule exist as unimer, while at increasing concentrations, aggregation takes place. In the review, we noticed that the gelation temperature of the polymer depends on polymer concentration. Increased concentration of the polymer decreases the gelation temperature. The micellar aggregates of the polymers depends a certain temperature. After a further temperature increase, it converted to gel due to micelles aggregation or packing. Therefore with these polymers, it is possible to mix drugs in the sol state and at room temperature and the solution can be injected into the target tissue. The hydrophobic core of the polymer behaves as reservoirs, where drug molecules can be incorporated by chemical, physical or electrostatic interactions depending on physicochemical properties.[19]

Bioadhesion can be defined as the process by which a natural or synthetic polymer can be adhered to biological substrate. When a biological substrate is a mucosal layer then the phenomena is known as mucoadhesion. The mucoadhesive polymers are Carbopol 934, Polycarbophil, HPMC and so many other polymers. [20]

Mucoadhesion can be occurred in two steps.

1) Contact stage

2) Consolidation stage.

Contact stage is characterized by the contact between the mucoadhesive and the mucous membrane with spreading and swelling of the formulation, initiating its deep contact with the mucous layer.

In consolidation step, the mucoadhesive materials are activated by the presence of moisture. Moisture plasticize the system allowing the mucoadhesive molecules to break free and to link up by weak vander wall and hydrogen bond. Essentially, there are two theories explaining the consolidation step, the diffusion theory and the dehydration theory. According to the diffusion theory, the mucoadhesive molecules and the glycoproteins of the mucous mutually interact by means of interpenetration of their chains and the building of secondary bonds[21]. By adding a suitable polymer, inclusion and muco-adhesive polymer with PVK extract, we can prepare a suitable Ayurvedic formulation thermo- sensitive vaginal gel of PVK extract, which will be easy for application, no drug resistance and no adverse reaction. Also it will be cost effective.

CONCLUSION

In the coming days and at present bacterial and fungal resistant infection has become a global health challenge and threatening the health of society. Drug resistance is increasing day by day due to unnecessary misuse of the synthetic drugs and continuous use of the drug in resistant infection. So, existing anti-fungal, anti-bacterial drugs have become less effective. Due to this cause universal use of natural drug (Ayurvedic medicine) have increased. If the Ayurvedic formulation develop in accordance with the modern pharmaceutical process, it should increase the patient compliance, increase the efficacy of the drug by better bioavailability and also maintain the constant plasma level of drug by sustain release. So the above reviews are beneficial for the scholar to develop an Ayurvedic formulation *Panchavalkal kashaya* thermo-sensitive vaginal gel for uncomplicated leucorrhoea.

Acknowledgement

I would like to thank my HOD Dr.Khem Chand Sharma, my guide Dr.Usha Sharma, my co- guide Dr. Shuchi Mitra and my previous guide late Dr. Sushma Rawat for their guidance to prepare this article.

REFERENCES

1. EL. Sayed A, Ibrahim, Omer M Shaaban, Gihan Feth, Khaled M.A Hassancin, "Development and characterization of thermo-sensitive pluronic-based metronidazole in situ gelling formulation for vaginal application" in Acta Pharmaceutica. 24 March 2012; 62: 59-70.
2. Kurniawansyah insan sunan, Sopyan iyan, Wathoni nasrul, Fillah dasty latifa, Praditya rahadianti umi, "Application and characterization of in situ gel" International Journal of Applied Pharmaceutics, 04 Sep 2018; 10(6): 34-37
3. Deshkar Sanjeevani S., Patil Arun T, Poddar Sushil kumar S. "Development of thermo-sensitive gel of fluconazole for vaginal candidiasis" International Journal of Pharmacy and Pharmaceutical Sciences, 02 Dec 2016; 8(1): 391-398
4. B. Sri Devi, N. Swarnalata, "Prevalence of RTI/STI among reproductive age women (15-49 years) in urban slums of Tirupati town, Andhra pradesh", Health and Population- Perspectives and Issues. Nov 2007; 30 (1): 56-70
5. Umme Hani and H.G Shivakumar, "Development of Miconazole nitrate Thermosensitive Bioadhesive vaginal gel for vaginal candidia" American Journal of Advanced Drug Delivery, 2013; 1(3): 358-368
6. Nikhar Shital R, Bansode Deepali A, Mahadik Kakasaheb R, "Thermosensitive in situ gel of tinidazole in treatment of bacterial vaginosis" International Journal of Ayurveda and Pharma Research, January 2020; 8(1): 1-12.
7. Deshpande, A.A., Rhodes, C.T., Danish, M., 1992. "Intravaginal drug delivery" Drug Development and Industrial Pharmacy 20th Oct 2008; 18 (11-12): 1225–1279.
8. Ye- Tae Kim, Baek- Ki Shin, Garripelli Vivek Kumar, Jin-Ki-Kim, "A thermosensitive vaginal gel formulation with HPγCD for the pH- dependant release and solubilisation of amphotericin B" European Journal of Pharmaceutical Sciences, 9th Oct 2010; 41(2): 399-406.
9. Reicher, A.J., Leibovitz, E., Linder, N., "Liposomal amphotericin B (AmBisome) in the treatment of neonatal candidiasis in very low birth weight Infants. Clinical and Epidemiological Studies, August 2000; 28: 223–226
10. Ye- Tae Kim, Baek- Ki Shin, Garripelli Vivek Kumar, Jin-Ki-Kim, " A thermosensitive vaginal gel formulation with HPγCD for the pH- dependant release and solubilisation of amphotericin B" European Journal of Pharmaceutical Sciences, 9th Oct 2010; 41(2): 399-406
11. Erem Bilensoy, M. Abdur Rouf, Imran Vural, Murat Sen, and A. Atilla Hıncal "Mucoadhesive, thermosensitive, prolonged release vaginal gel for clotrimazole: β-cyclodextrin complex" AAPS Pharm Sci Tech June 2006; 7 (2): E38-E44.
12. Nikhar Shital R, Bansode Deepali A, Mahadik Kakasaheb R, "Thermosensitive in situ gel of tinidazole in treatment of bacterial vaginosis" International Journal of Ayurveda and Pharma Research, January 2020; 8(1): 1-12

13. Umme Hani and H.G Shivakumar, "Development of Miconazole nitrate Thermosensitive Bioadhesive vaginal gel for vaginal candidia" American Journal of Advanced Drug Delivery, 2013; 1(3): 358-368
14. EL. Sayed A, Ibrahim, Omer M Shaaban, Gihan Feth, Khaled M.A Hassancin, "Development and characterization of thermo-sensitive pluronic-based metronidazole in situ gelling formulation for vaginal application" in Acta Pharmaceutica. 24 March 2012; 62: 59-70.
15. Deshkar Sanjeevani S., Patil Arun T, Poddar Sushilkumar S. " Development of thermo-sensitive gel of fluconazole for vaginal candidiasis" International Journal of Pharmacy and Pharmaceutical Sciences, 02 Dec 2015; 8(1): 391-398
16. Joshi Jayashree, "Experimental & clinical studies on the use of modified Panchavalkal (an Ayurvedic formulation) in Leucorrhoea". Delhi, Government of India, CCRAS, Ministry of Health & Family Welfare, 2013, p.70
17. Ye- Tae Kim, Baek- Ki Shin, Garripelli Vivek Kumar, Jin-Ki-Kim, "A thermosensitive vaginal gel formulation with HPγCD for the pH- dependant release and solubilisation of amphotericin B" European Journal of Pharmaceutical Sciences, 9th Oct 2010; 41(2): 3
18. Phennapha Saokham, Chutimon Muankaew, Phatsawee Jansook, Thorsteinn Loftsson "Solubility of Cyclodextrins and Drug/ Cyclodextrin Complexes" www.mdpi.com/ journal/ molecules, 11 May2018;23:1161
19. Giulia Bonacucina, Marco Cespi, Giovanna Mencarelli, Gianfabio Giorgioni and Giovanni Filippo Palmieri, "Thermosensitive Self-Assembling Block Copolymers as Drug Delivery Systems, www.mdpi.com/journal/polymers, 19 April 2011; 3: 779-811.
20. Yadav Vimal K, Kumar Raj, Kumar Brajesh, "Mucoadhesive polymer: means of improving the mucoadhesive properties of drug delivery system", Journal of Chemical and Pharmaceutical Research, May2010; 2(5): 408-432'
21. Boddupalli Bindu M, Mohammed Zulkar N.K, Nath Ravinder A, Banji David, "Mucoadhesive drug delivery system: An overview", Journal of Advanced Pharmaceutical Technology & Research, 2010 Oct-Dec; 1(4): 381-387.

Cite this article as:
Kirtidhara Behera, Usha Sharma, Shuchi Mitra, Khem Chand Sharma. A Critical Review on Thermo-Sensitive Vaginal Gel for the Foundation of Preparing Thermo-Sensitive Vaginal Gel of PVK (Panchvalkal Kashaya) Extract. International Journal of Ayurveda and Pharma Research. 2022;10(3):133-139.
https://doi.org/10.47070/ijapr.v10i3.2223
Source of support: Nil, Conflict of interest: None Declared

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