INCORPORATION AND EVALUATION OF MANNITOL AS HUMECTANT IN GEL PREPARATIONS

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ABSTRACT

Humectant is defined as a substance that absorbs or helps another substance to retain moisture. It is often a molecule with several hydrophilic groups most often hydroxyl groups, but sometimes amines and carboxyl groups encountered as well the affinity to form hydrogen bonds with molecules of water. Humectants also elevate the hydration of the skin to minimize the dehydrating effect. Although humectants have applications in many industries like pharmaceutical, food, veterinary etc. but the focus here is on humectants in skin care cosmetics. The use of moisturizers is the mainstay of treatment for preventing the dryness of the skin and also for daily maintenance of normal skin. All moisturizer products contain a careful balance of humectants as ingredient to restore just the correct amount of hydration back to the body. Considering protection and maintenance of healthy skin, cosmetics are becoming more important in daily routine of life. They are used regularly by increasing number of people and very large quantities are consumed each year. So this gives a motivation to explore such ingredients for the products which will fulfill maximum expectations of consumers with safety. The present article main aim is to identify study and select such chemicals which works as a better humectant than commonly used humectant like glycerin. Also decide the concentration of the ingredient at which it shows its best efficiency of being humectant and have benefits over the common ingredients.

Keywords: Mannitol, Humectant, Hydrogel, Cosmetic, Trans Epidermal water Loss

1. INTRODUCTION

` The human skin is the outer covering of the body. It is the largest organ of the body weighing approximately 10 pounds and covering an area approximately of about 1.6 m2. The skin has multiple layers of ectodermal tissue and guards the underlying muscles, bones, ligaments and internal organs. Skin is responsible for protecting the internal organs from the toxic present in the external world. It also provides us with sensory information about the surroundings and is our first defense against invasion by bacteria, viruses and other harmful elements. The skin is also an excretory organ, removing toxins from the body via perspiration.

The skin divided into three layers called epidermis, dermis and subcutaneous. Various appendages like hair, nail, sweat glands etc. are also a part of skin.

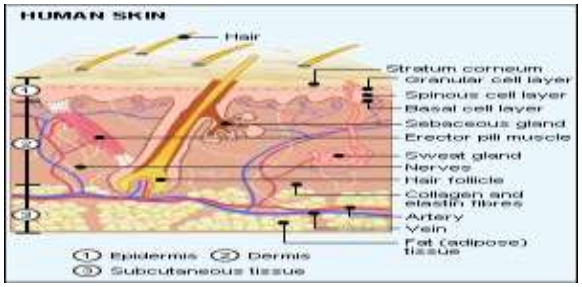


Figure 1: Structure of the Skin

1.1. Epidermis

The epidermis is composed of the outermost layers of cells in the skin. The epidermis is a stratified squamous epithelium 5 composed of proliferating basal and differentiated suprabasal keratinocytes which acts as the body major barrier against an external environment by preventing pathogens from entering into the body making the skin as a natural barrier. 6 It also regulates the amount of water released from the body. The epidermis is composed of several cell layers of about 0.1 mm – 0.3 mm thick.

1.2. Dermis

The dermis is composed of connective tissue below the epidermis. The convoluted surface of the dermis is in contact with the epidermis and the area where the epidermis protrudes downward into the dermis is called epidermis ridges. The area of the dermis near the epidermis protrusions is called the papillary dermis and the deeper dermis is called the reticular dermis. Unlike epidermis cells many of the dermal cells are not in tight cellular contact with each other and there are many extracellular spaces. This part of the skin that has a macromolecular network structure is called the extracellular matrix. 8

1.3. Subcutaneous Tissue

The sub cutis is the deepest layer of skin and is also known as the subcutaneous layer. The sub cutis, consisting of a network of collagen and fat cells helps conserve the body heat while protecting other organs from injury by acting as a shock absorber.

2. HUMECTANT

Humectants are frequently used in cosmetic formulations as a way of increasing and maintaining moisture of the skin and hair. The single or combinations of humectants are used in several cosmetic products including shampoo, conditioner, lotions, creams etc. 10 they are important cosmetic ingredients that prevents loss of moisture thereby retaining the skin's natural moisture balance. Some compounds like humectants have the ability to actively attract water from atmosphere. Humectants are key ingredients in most skin care products but are also often used in hair care products to volumize the hair by retaining moisture which expands the hair shaft. Humectant is defined as a substance that absorbs or helps another substance to retain moisture. It traps water molecules when applied to the skin and help in improving hydration of the stratum corneum. However the water that is drawn to the skin is trans epidermal water, as it continues evaporation from the skin can actually leads to dryness.

All humectants have hydroxyl groups which allow them to participate in hydrogen bonding and attract water. Various humectants have different ways of behaving because they differ in water binding capacity at different humidity. Humectants maintain water balance in the dermis by acting like a sponge that holds on water. Specifically humectants attract and hold on water provided by the dermis layer of skin. 12 Humectants are water loving agents often referred as hydrophilic ingredient in cosmetics. They are usually molecules with one or more hydrophilic groups attached to them. 13 These hydrophilic groups can be –

2.1. Hydroxyl Groups

A hydroxyl is a chemical functional group containing one oxygen atom connected by a covalent bonding to one hydrogen atom. The capacity of the hydroxy group to form hydrogen bonds imparts water solubility and internal structural. Some examples are like Propylene Glycol, Sorbitol 14

2.2. Amines

Amines are organic compounds and functional groups that contain a basic nitrogen atom with a lone pair. Amines are derivatives of ammonia, wherein one or more hydrogen atoms have been replaced by a

substituent such as an alkyl or aryl group. 15 Important amines include amino acids, biogenic amines. Some examples are like Hydroxyethyl urea, Sodium PCA etc16

2.3. Carboxyl Acids

It is an organic compound that contains a carboxyl group (C(O)OH). Carboxylic acids are polar because they are having both hydrogen-bond acceptors (the carbonyl -C=O) and hydrogen-bond donors (the hydroxyl -OH) they also participate in hydrogen bonding. Smaller carboxylic acids (1 to 5 carbons) are soluble in water Some example are like AHA alpha hydroxy acid

2.4. Role of Humectant

The humectant in cosmetics plays an important role that it serves as a moisture retaining agent of the products and also contributes the retention of stability of the system. A necessary condition for the humectant is that it can retain moisture for a long time without being influenced by environmental conditions like temperature, humidity, wind, etc. especially in humidity. For any humectant however the water absorption amount and moisture release amount are influenced by humidity due to relation of vapor pressure. In case of glycerin, equilibrium moisture content is 60% under the conditions of the temperature at 25°C and relative humidity of 75% Also in case of sorbitol, the equilibrium moisture content is 50% at a relative humidity of 75%. Humectants are cosmetic ingredient allow preventing loss of moisture thereby retaining the skin natural moisture. Normally up to 15% of the stratum corneum consists of Tran's epidermal water. When the moisture content of the stratum corneum falls below 10% then skin appears dry and flaky that leads to reduce flexibility of the skin. In case of dry skin the skin cells are being shed too fast rather than being shed individually these come off in clumps that look like white flakes. Repeated application of skin care products that is having humectant can normalize the shedding of the skin cells. The application of humectants lies in their ability to attract water in doing so they assume the role of the dermal hydrophilic components of the stratum corneum by being absorbed from the formulation to the stratum corneum.

This mechanism of rehydration of the stratum corneum is done by the use of humectants. Skin care products specifically formulated for the purpose of moisturizing the skin therefore formulations contain humectants with the aim of maintaining the hydration status of the stratum corneum. Another purpose to use humectants in topical doses form is to increase the solubility of chemically active ingredients to increase the ability to penetrate the skin. Thirdly humectants prevent the drying of formulation and make the product stable throughout its shelf life. That is why humectants are ingredient widely used in cosmetics, pharmaceuticals, personal care products.

3. HYPOTHESIS

The ingredients under study are better humectant than commonly used humectant like glycerin and can be used as humectant in skin care cosmetics.

4. MANNITOL

After going in the course of literature, it is revealed that mannitol can be able to fulfill the requirements of being humectant Mannitol also known as mannite it is a white, crystalline solid. Chemically it is 1,2,3,4,5,6-hexanehexol and having formula as C6H8(OH)6. 20 Mannitol is classified as a polyhydric alcohol that it is derived from a mannose by reduction. Mannitol and sorbitol are isomers the only difference being the orientation of the hydroxyl group on carbon 2.21 Polyhydric alcohol are defined as the sum of saccharide derivative in which a hydroxyl group replaces a ketone or aldehyde group.

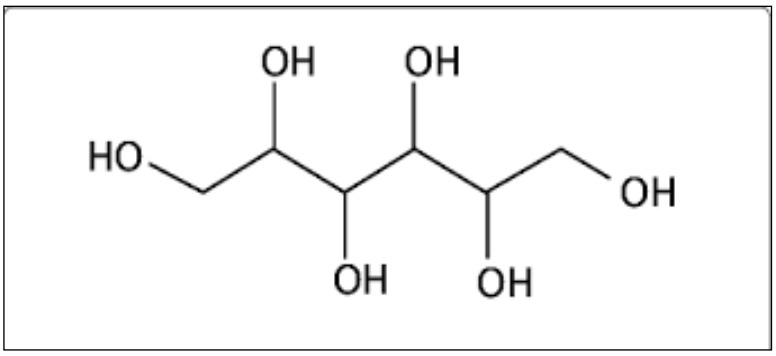


Fig 2 : Chemical Structure of Mannitol 22

4.1. Use of Mannitol

Mannitol is widely used in the food and pharmaceutical industries because of its unique functional properties.

In particular, it is about half as sweet as sucrose and when taken orally has a cooling effect which is considered desirable in masking bitter tastes.

5. MATERIALS AND METHODS

Skin care products are designed for improving skin conditions. Ideal skin care cosmetics protect the skin from the harmful effects of drying, atmospheric changes, UV radiations, etc. They are used to improve the appearance and health of skin; formulations are prepared for different types of skin and associated characteristics .24 Hydrogel was selected for the present study

5.1. Gel

A gel is a jelly like material that can have properties ranging from soft to hard. Gels are defined as a substantially diluted cross-linked system, which exhibits no flow when in the steady state. 25 Hydrogels is a gel in which the liquid component is water. Hydrogels are water swollen networks of hydrophilic homo polymers or copolymers. They are types of semisolid dosage form in which water is immobilized by polymers. The elements of hydrogels are water and a polymeric substance, hydrophilic polymeric networks in the presence of water hydrate and swell however dissolution is prevented by chemical cross links between the polymer chains.

5.2. Raw materials for formulation

5.2.1. Carbomer

Carbomer is generic name for synthetic high molecular weight polymers of acrylic acid. They may be homo polymers of acrylic acid, cross linked with an alkyl ether pentaerythritol, alkyl ether of sucrose or alkyl ether of propylene. The carbomer used in present gel formulation was ultrez.

5.2.2. Alkali

Triethanolamine often abbreviated as TEA, is a viscous organic compound and a strong base in nature that is both a tertiary amine and a triol. It is used to neutralizes fatty acids, adjusts and buffers the pH; it also solubilizes oils and other ingredients that are not completely soluble in water.

5.2.3. Preservative

The presence of microorganisms destroys the products. To prevent damages produced by microorganisms the preservative was used in the present gel formulation is sodium benzoate. 29

5.2.4. Solvent

Solvent forms a medium for dissolving the various components of the formulation. 30 In hydrogel water is used as solvent.

6. FORMULATION AND DEVELOPMENT

After selecting proper composition, the hydrogel was prepared. Hydrogel was prepared with Ultrez-21 polymer dispersed in water along with triethanolamine, sodium benzoate and active ingredient. After various trial and errors methods following composition was selected as final formulation and the ingredients were weighted for the preparation of formulations in Grams.

TABLE NO. 1: Hydrogel Formulation Containing Mannitol (M)

S. No	Ingredients	Function	M
1	Ultrez 21	Rehology Modifier	1.0
2	Tri ethanol amine	Neutralizer	0.6
3	Sodium Benzoate	Preservative	0.5
4	Mannitol	Active	1.0
5	Water	Solvent	Up to 100

6.1. Procedure of Formulation

Firstly all ingredients were weighed accurately. The solvent – water was taken in a beaker (Beaker A) and the carbopol (Ultrez 21) was sprinkled in it. After some time the carbopol was wet by the water. Then slowly with the help of glass rod, it was mixed carefully to get a uniform solution of water and carbopol with minimum aeration or lump formation. Triethanolamine was added to the beaker A for neutralization of the polymer. After that, sodium bicarbonate as preservative was incorporated to the beaker A along with slow stirring. Finally active ingredient was added to beaker A followed by uniform triturated to get the required gel product.

7. EVALUATION OF STABILITY PARAMETERS OF ACTIVE IN HYDROGEL FORMULATION

The stability of final formulation was observed at two different temperatures that is 45 + 2 oC and 10 + 2 oC. Various parameters such as Viscosity, pH and conductivity was observed. Accelerated stability studies and subjective evaluation was performed.

7.1. Viscosity

Viscosity is a measure of fluid's internal resistance to flow. It is calculated from a suitable spindle which is immersed in the test fluid through a calibrated spring. The viscous drag of the fluid against the spindle was measured by the spring deflection and it is calculated with a rotary transducer. Viscosity of the formulations was measured with Brookfield Viscometer. 31

7.2. pH

The pH is equal to −log10 c, where c is the hydrogen ion concentration in moles per liter. 32 pH of the formulations were measured with an instrument known as pH meter. A pH meter is a scientific instrument that measures the hydrogen-ion concentration in a solution indicating its acidity or alkalinity. The pH meter measures the difference in electrical potential between a pH electrode and a reference electrode. 33

7.3. Conductivity

The conductivity of a solution (K) is the reciprocal of resistivity (ρ) which is defined as the quotient of the electric field and the density of the current (flowing in the conducting solution). The resistance R (in Ω) of a conductor of cross-section S (in cm 2) and length L (in cm) is given by the expression

$$R = \rho \times L/S \text{ or } 1/K \text{ x } L/S;$$

thus, $K = 1/R \text{ x } L/S$

where, L/S corresponds to the ideal cell constant.34

7.4. Accelerated Stability Study

The evaluation of hydrogel was done in order to observe their stability for that they were subjected to accelerated stability testing to study the shelf-life of the formulations having active. 35

7.5. Subjective Evaluation

Determination of moisturizing activity of gel formulation was done by calculating the moisture retention capacity. Moisturizers have been used to alleviate dry skin; they reduced transepidermal water loss (TEWL) by promoting barrier repair, smooth exposed dermal nerve ending by creating temporary barrier and restore skin smoothness. Loss of water from the skin is known as trans epidermal water loss that was measured by using an instrument that is Cutometer. The principle on which cutometer works is to measure elasticity of the upper skin layer using negative pressure which temporarily deforms the skin mechanically. The parameters influencing the elasticity of the skin are moisture content, pressure and area of application. More is the moisturisation better is the elasticity. The pressure and area also plays an important role in the elastic property of skin.

8. RESULTS

Mannitol was showing very significant stable results of its viscosity, pH, conductivity and stability study that was observed at two different temperatures they were 45+2 oC and 10+2 oC. Subjective evaluations also indicated that volunteers were satisfied with the Trans Epidermal Water Loss capacity of the active.

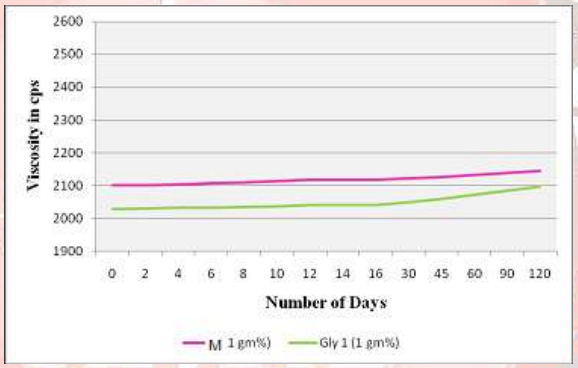
8.1. Viscosity

Viscosity indicates the consistency of the formulations. The observation shows that formulation kept at 45+ 2 oC temperatures had slight increase in the viscosity it may be due to the evaporation of water from the product. The formulation which was kept at 10 + 2 oC temperature shows almost constant readings till 30 days after that there were very minor changes in the observation of viscosity.

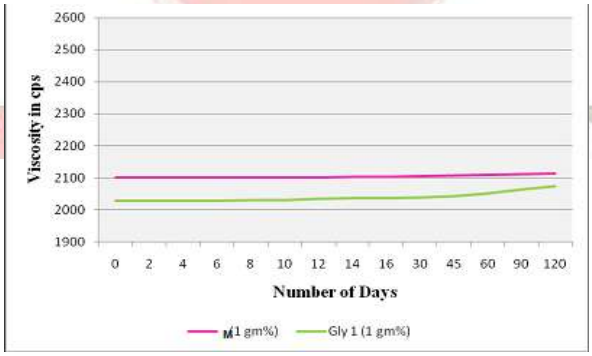
As in the experiment the two things were observed, firstly the pattern of viscosity of active throughout the study in the hydrogel formulation and secondly they were compared with glycerin at the same concentration in the hydrogel formulation. The both aspects were observed at two temperatures that were 45+ 2 oC and 10 + 2 oC. In the above mentioned aspects results obtained were observed and presented in following tables and graphs.

TABLE NO 2: The Comparative Values of Viscosity (cps) of Hydrogel Formulations having Mannitol and Glycerin at Same Concentration kept at 45 + 2 oC and 10 + 2 oC

No. of Days	M (45oC)	Gly (45oC)	M (10oC)	Gly (10oC)
0	2101	2029	2101	2029
16	2118	2042	2103	2036
30	2123	2049	2105	2038
45	2127	2060	2108	2046
60	2133	2072	2109	2051
90	2138	2084	2111	2064
120	2143	2092	2112	2075



Graph 1: The Comparative Values of Viscosity (cps) of Hydrogel Formulations having Glycerin and Mannitol at Same Concentration kept at 45 + 2 oC.



Graph 2: The Comparative Values of Viscosity (cps) of Hydrogel Formulations having Glycerin and Mannitol at Same Concentration kept at 10 + 2 oC.

8.2 .pH

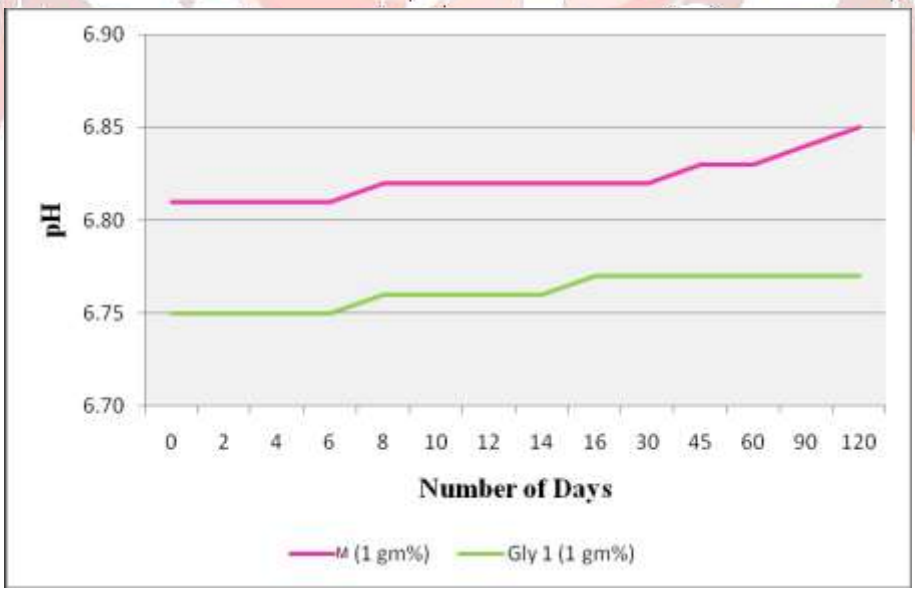
pH values determines the potential of hydrogen ions in the formulation. The observations shows that formulations kept at 45+ 2 oC temperature had slight variations in the pH it may correspond to the concentration

of hydrogen ions in the product. The formulations which was kept at 10 + 2 oC temperature shows almost constant readings till 14 days after that there was very negligible changes in the observations.

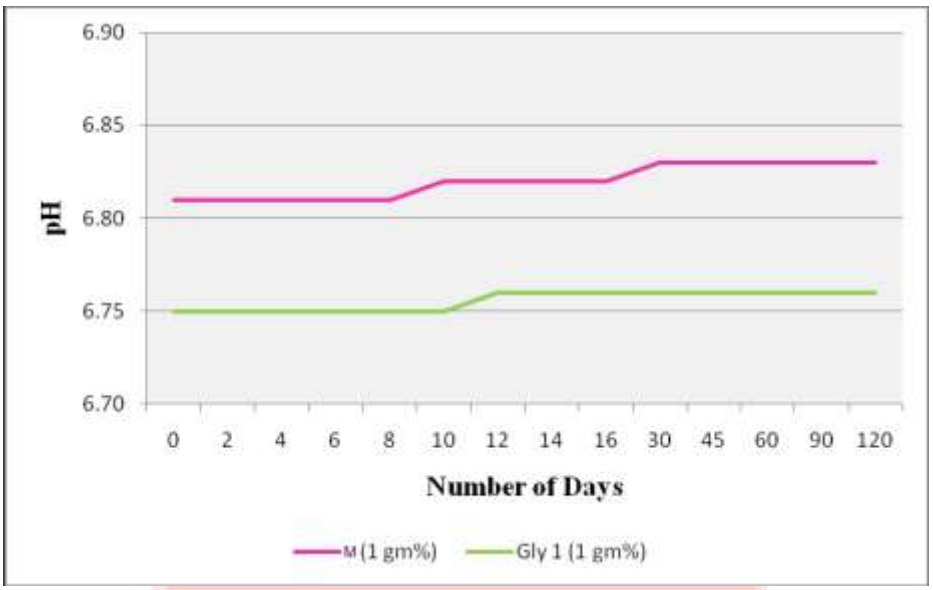
As we studied two aspects in the experiment that were first the pH value of active throughout the study in the hydrogel formulation and secondly, they was compared with glycerin at the same concentration in the hydrogel formulation. The both aspects were observed at two temperatures that were 45+ 2 oC and 10 + 2 oC. The results obtained from the observations are depicted in the subsequent tables and graphs

TABLE NO. 3: The Comparative pH Values of Gel Formulations having Mannitol and Glycerin at Different Concentrations kept at 45 + 2oC and 10 + 2 oC

No. of Days	M	Gly	M	Gly
	(45oC)	(45oC)	(10oC)	(10oC)
0	2101	2029	2101	2029
16	2118	2042	2103	2036
30	2123	2049	2105	2038
45	2127	2060	2108	2046
60	2133	2072	2109	2051
90	2138	2084	2111	2064
120	2143	2092	2112	2075



Graph 3: The Comparative pH Values of Hydrogel Formulations having Glycerin and Mannitol at Same Concentration kept at 45 + 2 oC.



Graph 4: The Comparative pH Values of Hydrogel Formulations having Glycerin and Mannitol at Same Concentration kept at 10 + 2 oC.

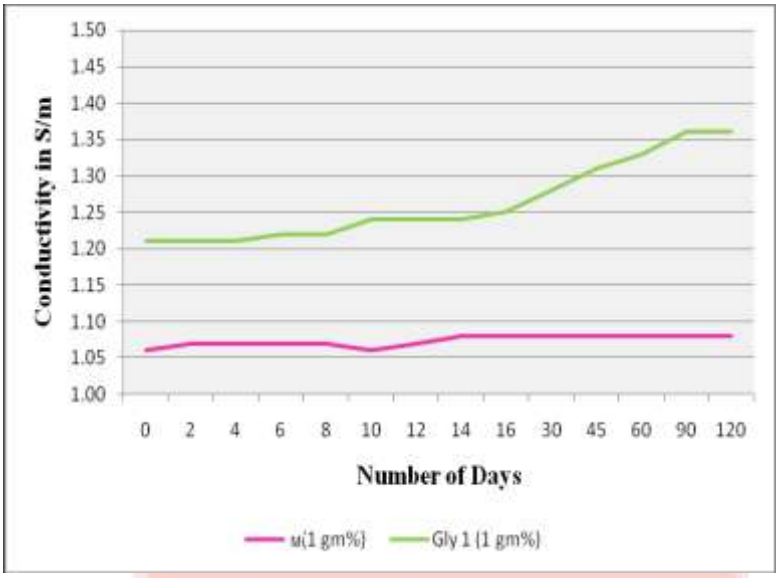
8.2. Conductivity

Conductivity is the measurement of the movement of the ions in the product. The gel formulation which was kept at 45+ 2 oC temperature shows slight increase in the conductivity of the products and is related to the change in the concentration of ions in the formulations under study. The formulations which were kept at 10 + 2 oC temperature shows almost stable readings.

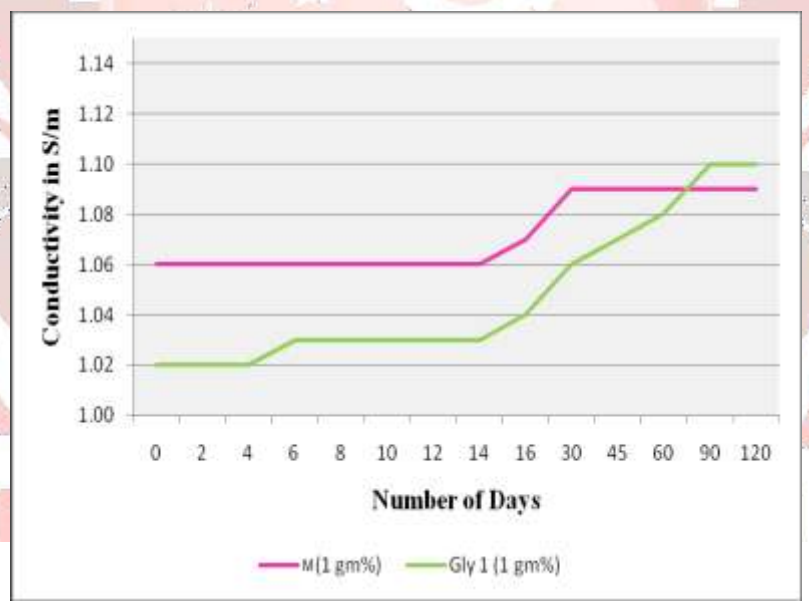
As we studied two aspects in the experiment those were first to observes the change in the conductivity of the hydrogel formulation and secondly they were compared with glycerin in the same concentrations of the hydrogel formulations. Both the aspects were observed at two temperatures 45+ 2 oC and 10 + 2 oC In all the aspects results obtained were observed and presented in table and graphs.

TABLE NO. 4: The Comparative Values of Conductivity (S/m) of Hydrogel Formulations having Mannitol and Glycerin at Different Concentrations kept at 45 + 2 oC and 10 + 2 oC

No. of Days	M	Gly	M	Gly
	(45oC)	(45oC)	(10 oC)	(10 oC)
0	1.06	1.21	1.06	1.02
16	1.07	1.25	1.06	1.02
30	1.08	1.28	1.07	1.03
45	1.08	1.30	1.09	1.04
60	1.08	1.33	1.09	1.06
90	1.08	1.33	1.09	1.08
120	1.09	1.36	1.09	1.10



Graph 5: The Comparative Values of Conductivity (S/m) of Hydrogel Formulations having Glycerin and Mannitol at Same Concentration kept at 45 + 2 oC.



Graph 6: The Comparative Values of Conductivity (S/m) of Hydrogel Formulations having Glycerin and Mannitol at Same Concentration kept at 10 + 2 oC.

8.3. Accelerated stability study

The stability of final formulations was observed at two different temperatures that is 45 + 2 oC and 10 + 2 oC. Various parameters such as color, odor, viscosity, pH and conductivity were studied. The evaluation of hydrogel formulation was done in order to determine their shelf-life. There was no significant change observed in above mentioned parameters of the products at 45 +2oC and 10 +2oC temperatures. Accelerated stability studies showed that formulations with active were stable during the period of study and observations are mentioned in the following table.

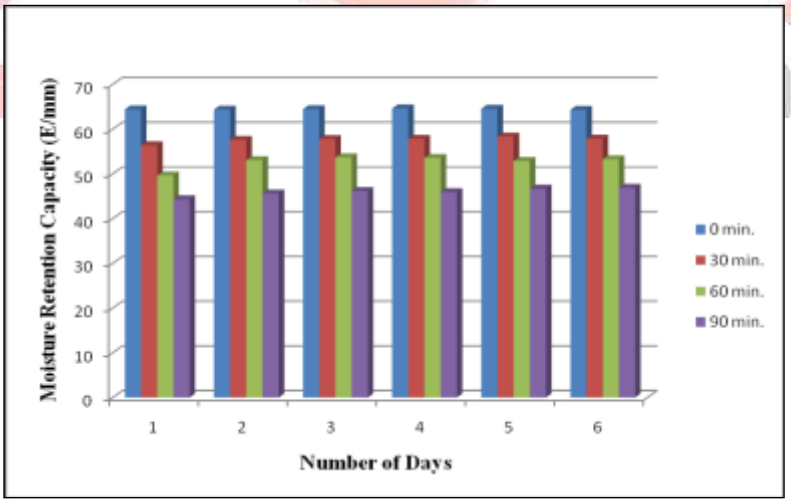
TABLE NO. 5: Accelerated Stability Study of Hydrogel Formulation having Mannitol at Different Parameters kept at 45+ 2oC and 10+ 2oC.

No. of Days	M	M	Gly	Gly
	(45oC)	(10oC)	(45oC)	(10oC)
	Colour	Odor	Colour	Odor
0	OC	OC	OC	OC
16	NC	NC	NC	NC
30	NC	NC	NC	NC
45	NC	NC	NC	NC
60	NC	NC	SDOC	NC
90	SDOC	NC	SDOC	SDOC
120	SDOC	SDOC	SDOC	SDOC

OC – Original Color, N C- No Change, S D O C- Slightly Dark of Original Color

8.5 Subjective Evaluation

Moisture retention result indicates that the hydrogel formulation with mannitol helps in reducing the trans epidermal water loss of the upper layer of skin. The volunteers were comfortable throughout the study. Readings obtained from subjective evaluations shows the positive results. The gel formulation with active was efficient in preventing Trans Epidermal Water Loss from the skin or increasing the moisturizer retention ability of the skin.



Graph 7: Showing the Values of Moisture Retention Capacity (E/mm) of Gel Formulation having Mannitol (M) (1 gm%) with respect to time (min.)

9. CONCLUSION

Mannitol is a sugar alcohol and it's a isomer of sorbitol so the hydrogel was formulated and evaluated for their physicochemical properties and to confirm whether it can be used in skin care cosmetic as a humectant. It was also subjected to stability study and subjective evaluations. During the study, formulation remained almost constant with very less fluctuation in the observed parameters. This indicates that the gel formulation is practically stable over an adequate time period. Mannitol come in the category of sugar alcohols; it is a isomer of sorbitol and having significant humectant property because the moisture retention results also indicates that the hydrogel formulation with mannitol helps in maintaing the moisture of the epidermis by reducing trans epidermal water loss. Along with that other parameters which were observed like viscosity, pH, conductivity and stability study. Hydrogel formulation having mannitol as an active was stable throughout the study.

Hence, it can be conclude that this study indicates that Mannitol can be successfully incorporated in hydrogel formulation and utilized for cosmetic purpose as they are exhibiting the humectant property in hydrogel formulation along with their other beneficial properties during the study.

REFERENCES

[1] Madison K C, et al ; Barrier Function of the Skin; Journal of Invest Dermatology; Natural Publishing Group London; 121(2); pp 231; 2003.

[2] Penzer R, Ersser S; Principles of Skin Care A Guide for Nurses and Health Care Practitioners; John Wiley & Sons New York; pp 12 ; 2010.

[3] Wilkson J B, Moore R J; Harry's Cosmeticology; George Godwin Great Britain; 7th ed.; pp 7; 1982.

[4] McCracken T; New Atlas of Human Anatomy; Academic Press London; pp 240 ; 2000.

[5] Sagarin E, Balsam M S; Cosmetic Science and Technology; Krieger Publishing Malabar Florida; pp 138 ; 1992.

[6] Mitsui T; New Cosmetic Science; Elsevier Science Amsterdam Netherlands; pp 53; 1997.