IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN: 2278-3008, p-ISSN:2319-7676. Volume 10, Issue 1 Ver. IV (Jan -Feb. 2015), PP 66-68
www.iosrjournals.org

The Relationship between Elasticity of Polymeric Gels and the In vitro Release of Medicaments

Mohamed Salama[1], Sharifah A. Alshatri[1], Amina Mohamed[2], Aref T. Mohamed[2], Eseldin I. Keleb[2], Assad A. Omar[2], Nagib A. Elmarzugi[2],[3],*

1Department of Pharmaceutics, Faculty of Pharmacy, Universiti Teknologi MARA, 42300 Bandar Puncak Alam, Selangor, Malaysia.
2Dept. of Industrial Pharmacy, Faculty of Pharmacy, Tripoli University and BioNano Integration Research Group, Biotechnology Research Center, LARST, Tripoli, Libya.
3Institute of Bioproduct Development, Universiti Teknologi Malaysia, Johor Bahru 81310, Johor, Malaysia.

Abstract: *Gels are semi-solid dosage forms that comprise small amount of solids dispersed in relatively large amount of liquid but still having solid-like structure. Rheological properties of gels may affect the release of proposed medicaments from the polymeric gels. The objective of this research was to find the relationship between the elasticity of polymeric gels and the in vitro release of Ketoconazole anti-fungal drug from different types of gel structures. Five types of gel bases were prepared, glycerin of starch, gelatin-glycerin, sodium carboxy methyl cellulose, Carbopol 934 and Eudragit L100. The rheological properties of gels were determined using Rheometer. Whereas the in vitro release of ketoconazole from the mentioned gel bases were determined using Franz Diffusion Cell. The results obtained showed that the higher the elasticity of the gel the more release of the drug.*

Keywords: *Elasticity, Viscosity, Gel bases, ketoconazole, Rheometer, Franz Diffusion Cell*

I. Introduction

Polymeric gels are formed from long disordered chains which are connected at specific points but the link should be reversible (das Neves and Bahia, 2006; Nagahata et al., 2014). Gels are produced through the cross-linking of polymer chains either by the formation of non-covalent bond which is physical cross linking or covalent bonds which is chemical cross linking (Bhasha et al., 2013). Hydrogels are differing from hydrophobic polymeric network, for instance poly-lactic acid that have limited capabilities of water-absorption. Hydrogels can absorb large quantities of water and at the same time remain insoluble in aqueous solution (Lin and Metters, 2006; Terech et al., 2006).

Gels are considers to exhibit non-Newtonian properties. Gels may be classified based a rheological properties, that the plot of rheogram gives yield value of gels above which the elastic gels distorts and begin to flow in some gel bases. However, the viscosity of some gels decreases with increasing rate of shear, with no yield value. The rheogram for gel material results from a shearing action on the long chain molecules of the linear polymers. As the shearing stress is increased, the disarranged molecules begin to align their long axis in the direction of flow with release of solvent from gel matrix (Jelvehgari and Montazam, 2011; Terech and Maitra, 2008).

The rheological properties of gels may affect their drug delivery and their consistency of treatment (Aminabhavi et al., 2004). Rheometer can be used to determine the rheological properties of the gels such as viscosity and elasticity (Sundaram et al., 2010). Rheometer can give the exact measurement of a complex substance’s response to an applied deformation (strain) or force (stress), and the rheological properties of the gels can be determined by oscillatory or flow rheometry (Pan et al., 2013).

These properties are mainly expressed by viscosity and elasticity of a gel is expressed as elastic (storage) modulus (G’) which is defined as the measurement of the ability of the gel to prevent deformation when pressure is applied (Fujii et al., 2000). Elasticity of gels has been proven as the most characteristic feature distinguishing gels from other products (Salama et al., 1975). Rheological properties of gels may affect the delivery of drugs from them moreover may affect their application to the site of action and their consistency in treatment (Azarmi et al., 2007). Rheological properties of dosage form for example gels may affect their drug delivery system. Subsequently, the rational of the current study was to investigate the effect of elasticity of gels on the drug release property. Furthermore, rheological behavior of gels may affect its application to the site of action and their consistency of treatment in conjunction with the delivered dose.

II. Methodology

1. Preparation of gel bases

Five types of gel bases were prepared; these are glycerin of starch gel, gelatin glycerin gel, sodium carboxy methyl cellulose gel, Carbopol 934 gel and Eudragit L100gel. Glycerin of starch gel bases are consisting of wheat starch (85 gm), glycerol (170 gm) and 745 ml of water, the glycerin heated (not more than 140 ºC) mixed the water and wheat starch under stirrer. Gelatin glycerin gel bases are consisting of glycero-gelatin in water containing 2% of gelatin and 70% of glycerin. Sodium carboxy methyl cellulose gel bases 5% dissolved in water until homogenous gel obtained. Carbopol 934 2% dissolved in water and the pH was adjusted to 5.5 by addition of triethanolamine to obtain the suitable gel. Eudragit L 100 30% was added in ethyl alcohol and stirred by a homogenizer until completely dissolved. After the preparation of all gel bases formulations, 1% ketoconazole was incorporated in each gel base for further study.

2. Rheological properties of the medicated gels

Rheological analysis was conducted by a Rheometer (Physica MCR301, AntonPaar GmbH, Stuttgart, Germany) with cone and plate geometry sensor (50mm diameter, 1º cone angle). Samples of gel bases were measured at 23±3 ºC. The frequency range was set between 0.1 and 100Hz. The elasticity of gels was determined by measuring the storage modulus (elasticity), loss modulus and complex viscosity. The gels was applied for non-medicated gel. Ketoconazole was dissolved in ethyl alcohol at different concentration to get the standard calibration curve and the absorption was determined by using UV spectrophotometer at 269nm.

3. Determination of in vitro release

In vitro release of ketoconazole analysis was done by Franz Diffusion Cell, using cellulose acetate membrane (25 mm & 45um pore size). Phosphate buffer pH 7 and 32ºC for 3 hours with hourly interval sample withdraw, and measuring the absorbance by UV spectrophotometer at 296nm.

III. Results And Discussion

Although, it is critical to know the exact value of the elastic modulus of the bulk gels, can be evaluated with a variety of techniques and systems. From the application of tensile stresses to gel slabs using clamps and weights, to specialized extension or compression machines, to measurements of gel deformations under shear in rheometers and to measurements of indentations produced by heavy beads or use of specialized microindenters (Boudou et al., 2006; Gutierrez and Groisman, 2011). However, different gel bases were characterized and tested for their elasticity properties. The obtained results, which illustrated in table 1, show that the higher elastic form of gel bases are glycerin of starch gel base have released the highest amount of ketoconazole. However, Eudragit L100 showed the lowest elasticity and released amount of ketoconazole. The tested gel bases can be arranged in the following descending order according to the release of ketoconazole:

Glycerin of starch, carbopol934 > glycerol-gelatin > sodium carboxy methyl cellulose > EudragitL100. These results may be due to the strength of intermolecular attraction bonds occurring within the gel base that facilitates drug release (Naresh et al., 2015). Figure 1 shows the relationship between the elasticity of gel bases and the amount of ketoconazole released after 3 hours. A direct relationship between the rheological properties of gel bases and the release of medicaments can be distinguished. This stress on the importance of parameter of elasticity and its effect on release of therapeutic materials to targeted site of action on the proper duration physicochemical properties of ketoconazole as a hydrophobic may has another effect, which may be differ from those incorporated medicaments of hydrophilic nature.

The elastic modulus of gels may affect the molecular weight and the concentration of gel with cross-linking. Nevertheless, variations of the gel elastic moduli due to structure and preparation variations of the cross-linking conditions. Therefore, the reliance on the published data cannot completely substitute for direct measurements of specific samples of gels. The literature data on the elastic moduli of some types of gels is generally scarce, and no coherent recipe for continuous (Gutierrez and Groisman, 2011; Peyton and Putnam, 2005).

IV. Figures and Tables

Table 1 shows the rheological properties of the gel bases

Gel base	Storage Modulus (Elasticity)[Pa] ($x10^3$)	Loss Modulus (Viscosity)[Pa]	Amount of ketoconazole released after 3 hours x 10^3mg
1. Glycerin of starch	26.4	6230	2.844
2. Carbopol 934	3.38	665	1.047
3. Glycero-gelatin	2.8	538	0.919
4. Sodium CMC	2.11	1410	0.630
5. Eudragit L100	0.802	754	0.236

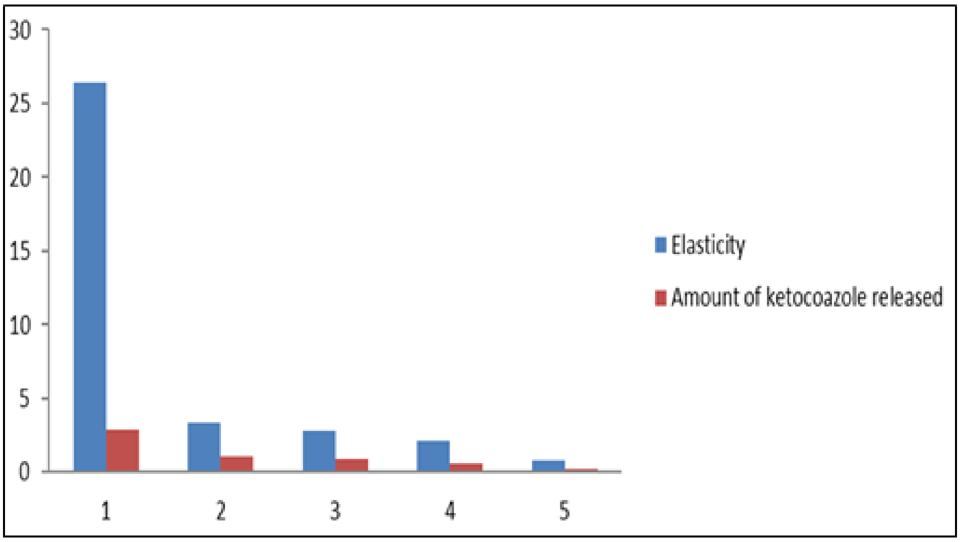

Figure 1 The relationship between the elasticity of gel bases and the amount of ketoconazole released after 3 hours

V. Conclusion

The elasticity properties of gel bases play an important role in characterizing the release of therapeutic materials from its carrier. The rheological properties of medicated polymeric gels greatly affect the in-vitro release of medicament from gel bases. The higher elastic form of examined gels have released the greater amount of ketoconazole. Glycerin of starch gel show the highest value of elasticity and greater release of incorporated drug. However, Eudragit L100 gel base show the lowest value of elasticity and minimum release of incorporated drug. Further in vivo studies are advised to illustrate the observation of longer effect of elasticity on release of incorporated medicaments.

References

[1]. T.M. Aminabhavi, S.A. Agnihotri and B.V.K. Naidu, Rheological Properties and Drug Release Characteristics of pH-Responsive Hydrogels, Journal of Applied Polymer Science 94 (2004), pp. 2057-2064.
[2]. S. Azarmi, W. Roa and R. Löbenberg, Current perspectives in dissolution testing of conventional and novel dosage forms, International Journal of Pharmaceutics 328 (2007), pp. 12-21.
[3]. S.A. Bhasha, S.A. Khalid, S. Duraivel, D. Bhowmik and K.P.S. Kumar, Recent Trends in Usage of Polymers in the Formulation of Dermatological Gels, Indian Journal of Research in Pharmacy and Biotechnology 1 (2013), pp. 161-168.
[4]. T. Boudou, J. Ohayon, Y. Arntz, G. Finet, C. Picart and P. Tracqui, An extended modeling of the micropipette aspiration experiment for the characterization of the Young's modulus and Poisson's ratio of adherent thin biological samples: Numerical and experimental studies, Journal of Biomechanics 39 (2006), pp. 1677-1685.
[5]. J. das Neves and M.F. Bahia, Gels as vaginal drug delivery systems, International Journal of Pharmaceutics 318 (2006), pp. 1-14.
[6]. T. Fujii, T. Yano, H. Kumagai and O. Miyawaki, Scaling Analysis of the Concentration Dependence on Elasticity of Agarose Gel, Bioscience, Biotechnology, and Biochemistry 64 (2000), pp. 1618-1622.
[7]. E. Gutierrez and A. Groisman, Measurements of Elastic Moduli of Silicone Gel Substrates with a Microfluidic Device, PLoS ONE 6 (2011), p. e25534.
[8]. M. Jelvehgari and H. Montazam, Evaluation of Mechanical and Rheological Properties of Metronidazole Gel as Local Delivery System, Arch Pharm Res 34 (2011), pp. 931-940.
[9]. C.-C. Lin and A.T. Metters, Hydrogels in controlled release formulations: Network design and mathematical modeling, Advanced Drug Delivery Reviews 58 (2006), pp. 1379-1408.
[10]. T. Nagahata, H. Yamaguchi, H. Monzen and Y. Nishimura, The Use of Polymer Gel Dosimetry to Measure Dose Distribution Around Metallic Implants, Japanese Journal of Radiological Technology 70 (2014), pp. 1160-1165.
[11]. Y. Naresh, C.R. Baru, V. S and R. Sasidhar, Formulation Design and Characterization of matrix Tablets of Lamivudine, Indo American J of Pharm Sci 2 (2015), pp. 514-522.
[12]. Y. Pan, X.S. Chan and L. Li, Rheological Study on the Gel-like Behaviour: Effect of Interfecial Adhesion, Journal of The Society of Rheology Japan 41 (2013), pp. 121-128.
[13]. S.R. Peyton and A.J. Putnam, Extracellular matrix rigidity governs smooth muscle cell motility in a biphasic fashion, Journal of Cellular Physiology 204 (2005), pp. 198-209.
[14]. M. Salama, A. A. and G.I. Ya., A study of the Effect of Rheological Properties of Gelatoglycerin Bases on the Resorption of Medicinal Substances, Pharmazie 4 (1975).
[15]. H. Sundaram, B. Voigts, K. Beer and M. Meland, Comparison of the Rheological Properties of Viscosity and Elasticity in Two Categories of Soft Tissue Fillers: Calcium Hydroxylapatite and Hyaluronic Acid, Dermatologic Surgery 36 (2010), pp. 1859-1865.
[16]. P. Terech and U. Maitra, Structural and Rheological Properties of Aqueous Viscoelastic Solutions and Gels of Tripodal Cholamide-Based Self-Assembled Supramolecules, J. Phys. Chem. B 112 (2008), pp. 13483-13492.
[17]. P. Terech, N.M. Sangeetha and U. Maitra, Molecular Hydrogels from Bile Acid Analogues with Neutral Side Chains: Network Architectures and Viscoelastic Properties. Junction Zones, Spherulites, and Crystallites: Phenomenological Aspects of the Gel Metastability, J. Phys. Chem. B 110 (2006), pp. 15224-15233.