Kerbala Journal of Pharmaceutical Sciences

ISSN: 2221-7207(Print) / **ISSN**: 3006-7189 (Online)

Formulation and Evaluation of Apigenin-Loaded Topical Organogel for the Wound Healing

Athmar Dhahir Habeeb Alshohani[1] *

[1]Department of Pharmaceutics, College of Pharmacy, Mustansiriyah University

***Corresponding Author:**
Athmar Dhahir Habeed Alshohani: athmar1978@uomustansiriyah.edu.iq

Received: 02/09/2025
Accepted: 10/10/2025
Published: 31/12/2025

Keywords: Wound healing, Apigenin, Lecithin and organogel

Abstract

Wound healing is a complicated process that requires the use of many medications including anti-inflammatory and antioxidants. A naturally occurring flavonoid, apigenin can be found in a variety of fruits, vegetables, and medicinal plants that has versatile benefits and medical uses including wound healing, antioxidant, antiaging and others. Organogel is one of the promising topical drug delivery strategies which have many potentials in drug delivery effect. Organogel will be used for the topical delivey of apigenin. Different organogels were prepared by using lecithin, isopropyl myristate, pluronic F127, PEG 400 and water. The formulations were evaluated for their gelation temperature, pH, drug content, viscosity and drug release. The results demonstrated that without PEG 400 only 55% of the drug was released after 6 hours while 91% was released when PEG 400 was used. Formulation F5 was the optimum formula with appropriate viscosity (3372 mPs), pH (6.33), drug content (91%) and 27°C gelation temperature. Drug release was around 91% within 6 hours. The formulated APN topical organogel will have the potential to improve wound healing by delivering the medication to the wound site in a sustained and localized approach.

DOI: 10.62472/kjps.v16.i27.147-156

تشكيل وتقييم جل عضوي موضعي محمل بالأبيجينين لشفاء الجروح

أثمار ظاهر حبيب

الخلاصة

يمكن أن يؤثر العمر والاضطرابات الأيضية والالتهابات وعوامل أخرى على عملية التئام الجروح المعقدة. يمكن العثور على الأبيجينين، وهو فلافونويد طبيعي، في مجموعة متنوعة من الفواكه والخضروات والنباتات الطبية التي لها فوائد متعددة واستخدامات طبية بما في ذلك التئام الجروح ومضادات الأكسدة ومكافحة الشيخوخة وغيرها. يُعد الجل العضوي أحد استراتيجيات توصيل الأدوية الموضعية الواعدة التي تتمتع بإمكانات عديدة في تأثير توصيل الدواء. تم تحضير الجل العضوي المختلف باستخدام الليسيثين وميريستات الأيزوبروبيل والبلورونيك F127 والماء. تم إنتاج ثماني صيغ من الجل العضوي الأبيجينين ثم تم تقييمها في المختبر من حيث درجة حرارة التجلط ودرجة الحموضة ومحتوى الدواء واللزوجة وإطلاقها. أظهرت النتيجة أن الصيغة F5 هي الأفضل مع اللزوجة المناسبة ودرجة الحموضة ومحتوى الدواء ودرجة حرارة التجلط وإطلاق الأبيجينين 3372 ميلي باسكال و6.33 و99.4 و27 درجة مئوية و91٪ بعد 6 ساعات.

1. Introduction

Skin injuries are common because skin is the largest organ of the human body. It acts as a barrier between the internal and external environments, that is why it is continuously exposed to a variety of injuries such as cuts, abrasions, burns and infections. Wound healing after injury is a complex process and mainly require the use of anti-inflammatory agents among other medications needed (Pârvănescu et al., 2021). Natural substances termed flavonoids have demonstrated known anti-inflammatory and antimicrobial qualities that may aid in wound healing and have potential uses in wound care (Utpal et al., 2024). Apigenin (APN) is a naturally occurring flavonoid found in a variety of vegetables, fruits and several medicinal plants. The APN has been shown in numerous studies to have a wide range of therapeutic potential, including anti-inflammatory, anti-cancer, antioxidant, and antidiabetic properties as shown in Fig.1 (Majma Sanaye et al., 2022). It's clinical use is limited by its poor dissolution due to its highly lipophilic nature and very low aqueous solubility (Kazmi et al., 2022, Allemailem et al., 2024). Rajesh et al formulate APN as hydrogel for wound healing. It was noticed that wound contraction was significantly increased in the injured animals compared to the control group. On day 18 the APN hydrogel treated group was completely healed compared to the control which had only 86.25% healing after 20 days (Shukla et al., 2016). It has been also revealed that APN may improve tissue repair and wound healing in diabetic rat skin (Zhang et al., 2015).

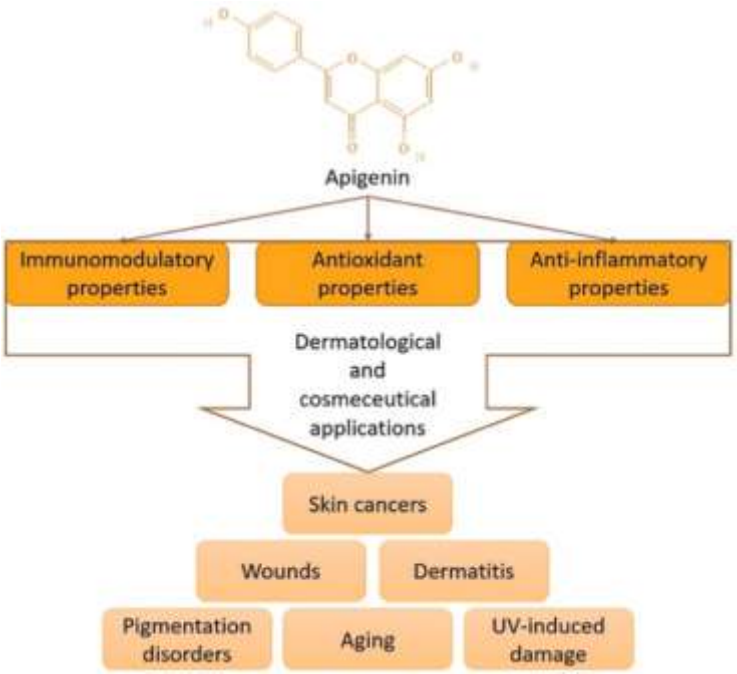

Figure1: Dermatological and Cosmeceutical Applications of Apigenin. Apigenin, a naturally occurring flavonoid, exhibits multiple biological activities, including immunomodulatory, antioxidant, and anti-inflammatory properties. These effects contribute to its potential dermatological and cosmeceutical applications, particularly in the management and prevention of skin cancers, wound healing, dermatitis, pigmentation disorders, skin aging, and ultraviolet (UV)-induced skin damage.

Topical drug delivery can be achieved using different drug delivery systems such as creams, ointments, gels, emulsions, hydrogels and organogels. Organogels are a promising class of topical drug delivery systems that have gained a lot of interest due to their potential to increase drug effectiveness by immobilizing the drug loaded to sustained release (Nishad et al., 2025). They are composed of gelators and polar solvent which are immobilized within the available spaces of a three-dimensional network system to form semisolid bicontinuous systems (Raut et al., 2024). They are divided into two categories: chemical and physical. The first kind is produced when covalent crosslinks interact to form chemical organogels during the gelation process. In contrast, physical type interacts by noncovalent cross-linking. They are made by the physical interactions and self-assembly of organogelator molecules without the need for permanent cross-linking. This type ideally, exhibit viscoelastic properties; involving sorbitan monostearate, microemulsion−gelatin-based, eudragit, limonene and pluronic lecithin organogels (Raut et al., 2024). Several studies demonstrated the effectiveness of using organogels for topical drug delivery in wound healings (Almeida et al., 2012). One of the widely used materials for organogel formulations are isopropyl myristate (IPM), soy lecithin (LN) and pluronic F127. IPM is an emollient that is non-oleaginous and has a high spreading capacity while LN is a naturally occurring combination of fatty acid diglycerides coupled with phosphoric acid choline esters. LN is also used as a penetration enhancer in the organogel. Pluronicc F127 strengthining the bond that hold the gel network together and stabilize the organogel formation process (Balata et al., 2014). In the current research, IPM, LN and Pluronic F127 will be used for organogel formulation in addition to studying the effect of PEG 400 on the organogel properties. This APN topical organogel will have the potential to improve wound healing by delivering the medication to the wound site in a sustained and localized approach.

2. Materials and Methods

2.1. Materials

Apigenin and Soy Lecithin were bought from bidepharm technology, China. PEG 400 and Sorbic acid (SA) were supplied from Baoji Guokang Bio-Technology CO., Ltd, China. Isopropyl myristate (IPM) obtained from ACMEC biochemical company, China. Whereas, Pluronic F127 was bought from BASF, Germany and Potassium sorbate (PS) have purchased from Henan GP chemical Co., Ltd., China.

2.2. Methods

2.2.1. Preparation of APN Pluronic LN Organogel

APN organogel was prepared utilizing three different phases which are drug phase, oil phase and aqueous phase and the quantities and materials used for each phase can be seen in Table1. The oil phase was prepared by dissolving soybean LN in IPM, which was used as a stabilizing, emulsifying, and dispersing agent. The mixture was then left overnight to allow the LN to completely dissolve followed by the addition of sorbic acid SA as preservative. For the preparation of aqueous phase, potassium sorbate and pluronic F127 were dissolved in cold water to create pluronic gel. The dispersion was then refrigerated at 2–4°C overnight to effectively dissolve Pluronic F127. For the preparation of the drug phase, APN was either dissolved in the oil phase or dissolved first in PEG 400 then the mixture was added into the LN-IPM solution (oil phase). PEG 400 serves as a moisturizer and co-solvent. Lastly, a mechanical stirrer was used to gradually introduced 70% aqueous phase to 30% oil phase while stirring at 400 rpm (Ba et al., 2016).

Table1: The APN Organogel Formulas

Formula Code	Ingredients (w/v %)							
	Drug Phase		Oil Phase			Aqueous Phase		
	APN	PEG 400	LN	SA	IPM QS	Pluronic F127	PS	Water QS
F1	1	-	1	0.2	30	25	0.2	70
F2	1	-	2	0.2	30	25	0.2	70
F3	1	-	3	0.2	30	25	0.2	70
F4	1	-	4	0.2	30	25	0.2	70
F5	1	5	3	0.2	30	25	0.2	70
F6	1	5	4	0.2	30	25	0.2	70
F7	1	5	5	0.2	30	25	0.2	70
F8	1	5	6	0.2	30	25	0.2	70
QS=sufficient quantity								

2.2.2. In-vitro Evaluation of APN organogel

2.2.2.1. Gelation Temperature Determination

Organogel (0.25 g) from each formulation was placed in a test tube and then the test tube was placed in water bath at 2°C. The temperature increased at a rate of 5°C per hour up to 50°C. At the end of each hour the tube was tilted 90 degrees and the meniscus was observed. The transition from sol to gel was recorded when the test tube meniscus did not move and the temperature at which the formulation's physical condition changed was known as the gelation temperature (Pandey et al., 2010, Belgamwar et al., 2008).

2.2.2.2. Viscosity Measuring

Atago viscometer (Atago, Japan) was used to measure the viscosity of the formulations prepared at 25°C. All the formulas were subjected to viscosity measuring test using spindle number 6 (Agrawal et al., 2010).

2.2.2.3. pH measurement

Each formula was assessed for its pH using Hanna pH meter (Hanna, India). The electrode was immersed in each formula and the pH was recorded (Esposito and Kirilov, 2021).

2.2.2.4. Drug Content

For each formulation, 0.5 g of the organogel was mixed with 50 mL ethanol and stirred for one hour to ensure complete dissolve of the drug. After that the mixture was filtered via 0.45 mm syringe filters, the resultant solutions were subjected to spectrophotometric analysis for APN using a standard curve set at 336 nm (Fayez et al., 2015).

2.2.2.5. In-Vitro Release Study

The dissolution apparatus type II was used to study the drug release from the organogel. One gram of each formulation was placed into the dialysis bag (MW 12,000-14000Da), then into the dissolution apparatus jar filled with 200 ml of phosphate buffer pH 6.8 at 37°C. The study was conducted for 6 hours and a sample of 3 ml was withdrawn at specific times (15, 30, 45, 60, 90, 120, 180, 240, 300 and 360 min). Each time the withdrawn amount was replenished with the same amount of fresh buffer in order to maintain the sink condition. The samples were analyzed using spectrophotometer at APN UV lambda max 336 nm (Chauhan et al., 2024).

2.2.3. Statistical analysis

Significance was assessed using a one-way ANOVA, and a difference was deemed significant when $p<0.05$.

3. Results and Discussion

3.1. *In-Vitro* Evaluation of The Organogel

All the formulations were successfully prepared and had an opaque yellow color and homogeneous appearance.

3.1.1. Gelation Temperature

The organogel formulas gelation temperature was within the range of 21-35°C, as shown in Table2. The gelation temperature increased as the percentage of LN increased from F1to F4. The high concentration of LN will form dense matrix with strong interconnections that needs more energy to disturb the structure and to form an organogel. In addition, the formulations contained PEG 400 (F5 and F6) had higher gelation temperature compared that those free from PEG 400 and has the same LN percentage (F3 and F4). This increase in temperature can be explained by the fact that PEG 400 forms strong hydrogen bonding with LN leading to higher energy and temperature for the disruption of the LN bonding and formation of an organogel (Almeida et al., 2012).

3.1.2. Viscosity

The viscosity of the organogel is very important since it affects its spreadibility, flow property, patient compliance as well as the drug release. The produced organogel formulations showed viscosities range of 2873-3881 poise, as demonstrated in Table2. The viscosity measurement was under constant shear rate and temperature (37oC) which demonstrate non-Newtonian nature for the formulated gel. As the LN concentration raised, the viscosity of the formula increased and this could be due to the complex dense network formation in the gel. The viscosity also increased when PEG 400 was added (Rhee et al., 2006, Fakhari et al., 2017).

3.1.3. Ph Measurement

The formulas pH was within the range of 6.1-6.9 and this range was compatible with skin pH as skin afford this range. The pH measurement of the formula stated in Table 2. The results were about neutral and suitable for topical use without any irritation or discomfort (Ali and Yosipovitch, 2013, Dikstein and Zlotogorski, 1994).

3.1.4. Drug Content

APN amount in each formulated organogel was between 96.2-99.4% as demonstrated in Table2. The results of the APN content in the formulated gel demonstrated the active ingredient uniform distribution withing the base (Iwanaga et al., 2010, Dai et al., 2020).

Table2: The evaluation parameters for the organogel (n=3)

Formula Code	Gelation Temperature	Viscosity	pH	Drug Content
F1	21±0.5	2873±12	6.90±0.24	98.23±1.42
F2	23±1.0	2974±22	6.61±0.35	97.18±2.75
F3	24±0.5	3193±10	6.10±0.61	98.22±2.63
F4	27±0.0	3302±25	6.75±0.17	99.27±1.74
F5	27±0.5	3372±31	6.33±0.23	99.40±2.43
F6	29±0.0	3501±09	6.52±0.27	96.20±3.64
F7	33±0.5	3736±23	6.48±0.14	96.89±1.63
F8	35±0.5	3881±15	6.43±0.11	98.46±2.85

3.1.5. *In-Vitro* Release Study

The dissolution study was performed in order to explain the ability and amount of the APN release from the formulated organogel to be available topically in the required area Fig.2. Formulations with no PEG 400 had only around 35%,25%, 42% and 55% of the drug released within 6 hours for F1, F2, F3 and F4 respectively. The release was slowed as the LN concentration increased due to the formation of a denser gel matrix that hinder drug diffusion out of the ogranogel matrix (Franckum et al., 2004, Fayez et al., 2015). However, when PEG 400 was added, drug release was enhanced and the maximum amount of drug release reached 91% in 6 hours with F5 compared to 42 % in F3 without PEG 400. The process of APN release from the formulation relays on the drug solubility in the organogel and diffusion from the organogel. When PEG 400 was used it acted as cosolvent and enhanced drug solubility and dissolution, thus enhancing drug release (Bolourchian et al., 2013, Saharan et al., 2009, Vélaz et al., 1998). It was also noted that when LN concentration increased, drug release was slower in F6, F7 and F8 in spit of the presence of PEG 400 (Kumar and Katare, 2005, Jatav and Ramteke, 2015).

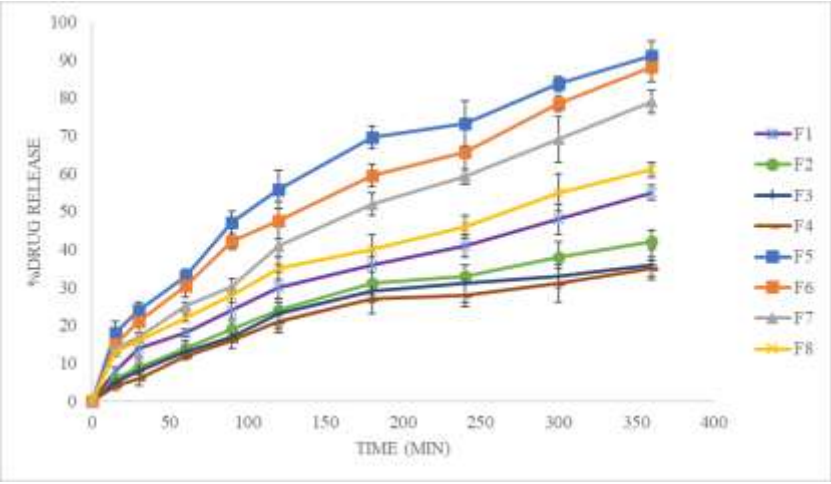

Figure2: In-vitro Drug Release Profiles of Formulations F1–F8. The figure illustrates the cumulative percentage of drug release (% drug release) from eight different formulations (F1–F8) as a function of time (0–360 min). All formulations exhibited a time-dependent increase in drug release, with noticeable differences in release rates and extents among formulations. Formulations F5 and F6 showed the highest cumulative drug release over the study period, whereas F1–F4 demonstrated comparatively slower release profiles. Data are presented as mean ± standard deviation (SD), as indicated by error bars.

4. Conclusion

Several APN organogels were prepared and compared regarding pH, viscosity, gelation temperature and drug release to be used in wound healing. Formulations F5 containing LN 3% (w/v), 25% pluronic F127 (w/v), 30% IPM (w/v) and 1% APN was chosen as the optimum formula because of the proper viscosity, pH and 91% of the drug was released within 6 hours. This could be a promising topical drug delivery strategy to enhance the topical delivery of APN for wound healing.

5. Conflicts of Interest: The authors declare no conflict of interest.

References

AGRAWAL, V., GUPTA, V., RAMTEKE, S. & TRIVEDI, P. 2010. Preparation and evaluation of tubular micelles of pluronic lecithin organogel for transdermal delivery of sumatriptan. *Aaps PharmSciTech,* 11**,** 1718-1725.

ALI, S. M. & YOSIPOVITCH, G. 2013. Skin pH: from basic science to basic skin care. *Acta dermato-venereologica,* 93**,** 261-267.

ALLEMAILEM, K. S., ALMATROUDI, A., ALHARBI, H. O. A., ALSUHAYMI, N., ALSUGOOR, M. H., ALDAKHEEL, F. M., KHAN, A. A. & RAHMANI, A. H. 2024. Apigenin: A Bioflavonoid with a Promising Role in Disease Prevention and Treatment. *Biomedicines,* 12.

ALMEIDA, H., AMARAL, M. H., LOBÃO, P. & LOBO, J. M. S. 2012. Pluronic® F-127 and Pluronic Lecithin Organogel (PLO): Main features and their applications in topical and transdermal administration of drugs. *Journal of Pharmacy & Pharmaceutical Sciences,* 15**,** 592-605.

BA, W., LI, Z., WANG, L., WANG, D., LIAO, W., FAN, W., WU, Y., LIAO, F. & YU, J. 2016. Optimization and evaluation of pluronic lecithin organogels as a transdermal delivery vehicle for sinomenine. *Pharmaceutical development and technology,* 21**,** 535-545.

BALATA, G., EL NAHAS, H. M. & RADWAN, S. 2014. Propolis organogel as a novel topical delivery system for treating wounds. *Drug Delivery,* 21**,** 55-61.

BELGAMWAR, V. S., PANDEY, M. S., CHAUK, D. S. & SURANA, S. J. 2008. Pluronic lecithin organogel. *Asian Journal of Pharmaceutics (AJP),* 2.

BOLOURCHIAN, N., MAHBOOBIAN, M. M. & DADASHZADEH, S. 2013. The effect of PEG molecular weights on dissolution behavior of simvastatin in solid dispersions. *Iranian journal of pharmaceutical research: IJPR,* 12**,** 11.

CHAUHAN, S., JHAWAT, V., SINGH, R. P., YADAV, A. & GARG, V. 2024. Design, Development and In-Vitro Characterization of Insulin Loaded Topical Pluronic-Lecithin Based Organogel Formulation for the Management of Diabetic Wound. *Recent Advances in Drug Delivery and Formulation: Formerly Recent Patents on Drug Delivery & Formulation,* 18**,** 50-60.

DAI, M., BAI, L., ZHANG, H., MA, Q., LUO, R., LEI, F., FEI, Q. & HE, N. 2020. A novel flunarizine hydrochloride-loaded organogel for intraocular drug delivery in situ: Design, physicochemical characteristics and inspection. *International journal of pharmaceutics,* 576**,** 119027.

DIKSTEIN, S. & ZLOTOGORSKI, A. 1994. Measurement of skin pH. *Acta dermato-venereologica. Supplementum,* 185**,** 18-20.

ESPOSITO, C. L. & KIRILOV, P. 2021. Preparation, characterization and evaluation of organogel-based lipstick formulations: Application in cosmetics. *Gels,* 7**,** 97.

FAKHARI, A., CORCORAN, M. & SCHWARZ, A. 2017. Thermogelling properties of purified poloxamer 407. *Heliyon,* 3.

FAYEZ, S. M., GAD, S., KHAFAGY, E., JALEEL, G., GHORAB, M. M. & EL-NAHHAS, S. A. 2015. Formulation and evaluation of etodolac lecithin organogel transdermal delivery systems. *Int J Pharm Pharm Sci,* 7**,** 325-34.

FRANCKUM, J., RAMSAY, D., DAS, N. G. & DAS, S. K. 2004. Pluronic lecithin organogel for local delivery of anti-inflammatory drugs. *International journal of pharmaceutical compounding,* 8**,** 101.

IWANAGA, K., SUMIZAWA, T., MIYAZAKI, M. & KAKEMI, M. 2010. Characterization of organogel as a novel oral controlled release formulation for lipophilic compounds. *International journal of pharmaceutics,* 388**,** 123-128.

JATAV, M. P. & RAMTEKE, S. 2015. Formulation and evaluation of lecithin organogel for treatment of arthritis. *Int J Sci World,* 3**,** 267-74.

KAZMI, I., AL-ABBASI, F. A., IMAM, S. S., AFZAL, M., NADEEM, M. S., ALTAYB, H. N. & ALSHEHRI, S. 2022. Formulation and Evaluation of Apigenin-Loaded Hybrid Nanoparticles. *Pharmaceutics,* 14.

KUMAR, R. & KATARE, O. P. 2005. Lecithin organogels as a potential phospholipid-structured system for topical drug delivery: a review. *Aaps Pharmscitech,* 6**,** 40.

MAJMA SANAYE, P., MOJAVERI, M. R., AHMADIAN, R., SABET JAHROMI, M. & BAHRAMSOLTANI, R. 2022. Apigenin and its dermatological applications: A comprehensive review. *Phytochemistry,* 203**,** 113390.

NISHAD, M., VERMA, S., KUMAR, A. & KHURANA, N. 2025. Formulation and evaluation of apigenin-loaded microsponge gel for effective angioedema therapy. *Current Pharmaceutical Analysis,* 21**,** 203-215.

PANDEY, M., BELGAMWAR, V., GATTANI, S., SURANA, S. & TEKADE, A. 2010. Pluronic lecithin organogel as a topical drug delivery system. *Drug delivery,* 17**,** 38-47.

PÂRVĂNESCU , R. D., WATZ, C.-G., MOACĂ, E.-A., VLAIA, L., MARCOVICI, I., MACAȘOI, I. G., BORCAN, F., OLARIU, I., CONEAC, G., DRĂGHICI, G.-A., CRĂINICEANU, Z., FLONDOR , D., ENACHE, A. & DEHELEAN, C. A. 2021. Oleogel Formulations for the Topical Delivery of Betulin and Lupeol in Skin Injuries—Preparation, Physicochemical Characterization, and Pharmaco-Toxicological Evaluation. *Molecules,* 26**,** 4174.

RAUT, S., AZHERUDDIN, M., KUMAR, R., SINGH, S., GIRAM, P. S. & DATTA, D. 2024. Lecithin Organogel: A Promising Carrier for the Treatment of Skin Diseases. *ACS Omega,* 9**,** 9865-9885.

RHEE, Y.-S., SHIN, Y.-H., PARK, C.-W., CHI, S.-C. & PARK, E.-S. 2006. Effect of flavors on the viscosity and gelling point of aqueous poloxamer solution. *Archives of pharmacal research,* 29**,** 1171-1178.

SAHARAN, V., KUKKAR, V., KATARIA, M., GERA, M. & CHOUDHURY, P. K. 2009. Dissolution enhancement of drugs. Part I: technologies and effect of carriers. *International Journal of Health Research,* 2.

SHUKLA, R., KASHAW, S. K., JAIN, A. P. & LODHI, S. 2016. Fabrication of Apigenin loaded gellan gum–chitosan hydrogels (GGCH-HGs) for effective diabetic wound healing. *International journal of biological macromolecules,* 91**,** 1110-1119.

UTPAL, B., SUTRADHAR, B., ZEHRAVI, M., SWEILAM, S., PANIGRAHY, U. P., URS, D., FATIMA, A., NALLASIVAN, P., CHHABRA, G., SAYEED, M. A., ALSHEHRI, M., RAB, S., SHARUK, K. & EMRAN, T. 2024. Polyphenols in wound healing: unlocking prospects with clinical applications. *Naunyn-Schmiedeberg's Archives of Pharmacology,* 398**,** 2459-2485.

VÉLAZ, I., SÁNCHEZ, M., MARTIN, C. & MARTÍNEZ-OHÁRRIZ, M. 1998. Effect of PEG 4000 on the dissolution rate of naproxen. *European journal of drug metabolism and pharmacokinetics,* 23**,** 103-108.

ZHANG, Y., WANG, J., CHENG, X., YI, B., ZHANG, X. & LI, Q. 2015. Apigenin induces dermal collagen synthesis via smad2/3 signaling pathway. *Eur J Histochem,* 59**,** 2467.