Global Academic Journal of Pharmacy and Drug Research

Available online at https://www.gajrc.com
DOI: https://doi.org/10.36348/gajpdr.2026.v08i06.003

OPEN ACCESS



ISSN (P): 2706-9044
ISSN (O): 2707-255X

Original Research Article

Carbopol 934 Ethosomal Gel of Quercetin: Physicochemical Properties and Release and Permeation across Excised Rat Skin Compared with a Plain Drug Gel

Raghvendra Chaubey[1]*, I. K. Yadav[1], Jitendra Kumar Malik[1]
[1]Faculty of Pharmacy, P.K. University, Shivpuri, M.P. India

***Corresponding Author**
Raghvendra Chaubey
Faculty of Pharmacy, P.K. University, Shivpuri, M.P. India

Article History
Received: 21.09.2026
Accepted: 17.11.2026
Published: 20.11.2026

Abstract: A liquid vesicle dispersion is awkward to apply to the skin. Putting the vesicles into a gel makes them easier to handle and keeps them where they are applied. We incorporated quercetin-loaded ethosomes (batch QEF-5, described in a companion paper) into a Carbopol 934 gel neutralised with triethanolamine and studied the product for pH, viscosity, spreadability, and release and permeation across excised rat skin in a Franz diffusion cell, using a plain quercetin gel as comparison. The carbomer base had a pH of 7.3 and a viscosity of about 73,400 cP; the ethosomal gel had a pH of 7.9 and about 75,100 cP, so adding the vesicles hardly changed the consistency. The spreadability value was 15.69 g·cm/s. Quercetin appeared in the receptor faster from the ethosomal gel than from the plain gel at every time point. After 24 h the cumulative amounts were 81.97% and 53.93%, and after 48 h 90.47% and 62.37%. The ethosomal gel showed a marked early phase (33.53% in the first hour) followed by a slower phase. Kinetic fits favoured first-order release for the ethosomal gel (R^2 0.955), while the plain gel was best described by the Higuchi equation (R^2 0.930). The Korsmeyer–Peppas exponent was about 0.23 for the ethosomal gel (first five points) and 0.85 for the plain gel. The ethosomal gel therefore moved more quercetin across the skin membrane over 48 h, but the high pH, the early burst and the lack of replicate data and of skin-retention measurements are points that need attention in further development.

Keywords: Quercetin, Ethosomal Gel, Carbopol 934, Franz Diffusion Cell, Release Kinetics, Topical Delivery.

Copyright © 2026 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution **4.0 International License (CC BY-NC 4.0)** which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

1. INTRODUCTION

Ethosomes are phospholipid vesicles containing ethanol, and they are widely studied for skin delivery because the ethanol makes the bilayer flexible and also loosens the packing of lipids in the stratum corneum (Touitou *et al*., 2000; Godin & Touitou, 2004). In our companion paper we prepared quercetin ethosomes by the cold method and picked one batch, QEF-5, for further work. A vesicle suspension is, however, hard to apply to the skin: it runs off, it is difficult to dose, and it is not pleasant to use. Incorporating the vesicles into a gel deals with these problems and gives a form that can be spread, left on the skin and packed in a tube (Mbah *et al*., 2014).

Carbopol (carbomer) polymers are a common choice for such gels. They are cross-linked acrylic acid polymers that swell in water and thicken sharply when their carboxyl groups are neutralised

Citation: Chaubey, R., Yadav, I. K., & Malik, J. K. (2026). Carbopol 934 Ethosomal Gel of Quercetin: Physicochemical Properties and Release and Permeation across Excised Rat Skin Compared with a Plain Drug Gel. *Glob Acad J Pharm Drug Res, 8*(6), 117-121. https://doi.org/10.36348/gajpdr.2026.v08i06.003

with an amine such as triethanolamine. A gel base for vesicles must satisfy a few conditions. Its pH should be tolerated by the skin, its viscosity should be high enough to stay in place but low enough to spread, and it should not break the vesicles or hold the drug back too strongly. Gels of ethosomes have been described for several drugs, among them anthralin (Fathalla *et al*., 2020), and reports on quercetin in vesicular systems are growing (Ferrara *et al*., 2022).

The release of a drug from a topical vesicular gel is usually followed in a Franz diffusion cell. In a set-up that uses excised skin, what is measured is the amount that arrives in the receptor, and so it combines release from the vehicle with passage across the skin (Barry, 2001). The shape of the curve is often analysed with simple kinetic models, with the Higuchi equation for diffusion from a matrix and the Korsmeyer–Peppas power law for the type of transport (Higuchi, 1963; Korsmeyer *et al*., 1983; Ritger & Peppas, 1987; Costa & Sousa Lobo, 2001). Here we describe how the ethosomal gel was prepared, how it behaved in simple physical tests, and how its release and permeation profile compared with that of a plain quercetin gel.

2. MATERIALS AND METHODS

2.1 Preparation of the Gel

Carbopol 934 was dispersed gradually in purified water under constant stirring and left to hydrate fully to give a uniform base. A series of six gels (QEG1–QEG6) containing 1.0 to 3.5% Carbopol 934 with 0.5% triethanolamine was prepared to explore the effect of polymer concentration (Table 1). The ethosomal suspension (QEF-5, equivalent to 20 mg of quercetin) was added slowly to the hydrated base under gentle stirring so that the vesicles were spread evenly, and the pH was brought to about 7.0 with triethanolamine. The gel was left to equilibrate. A plain quercetin gel was prepared as a comparison.

Table 1: Composition of the quercetin ethosomal gel series

Gel	Ethosomal suspension (equiv. to quercetin, mg)	Carbopol 934 (%)	Triethanolamine (%)	Phosphate buffer pH 7.4
QEG1	20	1.0	0.5	q.s.
QEG2	20	1.5	0.5	q.s.
QEG3	20	2.0	0.5	q.s.
QEG4	20	2.5	0.5	q.s.
QEG5	20	3.0	0.5	q.s.
QEG6	20	3.5	0.5	q.s.

2.2 Physicochemical Evaluation

For pH, 1 g of gel was dispersed in 100 mL of distilled water and the pH was read with a calibrated digital meter, in triplicate. Viscosity was measured on a Brookfield viscometer and given in centipoise. Spreadability was found by the glass-slide method: a fixed amount of gel was placed between two slides under a set weight, the time taken for the upper slide to slip off was noted, and spreadability was calculated as S = M·L/T, where M is the weight on the upper slide, L the length of spread and T the time. Homogeneity and grittiness were judged by rubbing a small amount between finger and thumb.

2.3 Release and Permeation across Rat Skin

Release and permeation were studied in Franz diffusion cells with dorsal skin from healthy young rats (5–6 weeks old; hair removed, skin cleaned and equilibrated) as the membrane, the stratum corneum facing the donor compartment. One gram of gel was placed in the donor compartment. The receptor held 28 mL of phosphate-buffered saline (pH 7.4) at 37 ± 1 °C with magnetic stirring. Five-millilitre samples were withdrawn at set intervals and replaced with fresh buffer to maintain sink conditions, and quercetin was measured by UV spectrophotometry at 246 nm against a buffer blank. The plain quercetin gel was run in the same way. Results are given as cumulative percentage of the drug reaching the receptor.

2.4 Kinetic Analysis

The mean cumulative percentage values were fitted to the zero-order (Q against t), first-order (log of percentage remaining against t) and Higuchi (Q against $\sqrt{t}$) equations by linear regression, and R^2 was compared. For the Korsmeyer–Peppas model, log Q was plotted against log t for the part of the curve up to about 60% release, and the slope was taken as the exponent *n*. For a planar system, *n* of about 0.5 indicates Fickian diffusion, values between 0.5 and 1.0 indicate anomalous transport, and a value near 1.0 indicates release controlled by relaxation of the matrix (Ritger & Peppas, 1987). Time zero was left out of all the regressions.

3. RESULTS AND DISCUSSION

3.1 Physical Properties of the Gel

The ethosomal gel was smooth and homogeneous to the touch. Its pH and viscosity are shown in Table 2, together with those of the plain carbomer base. Incorporation of the vesicles raised the viscosity only slightly, from about 73,400 to

75,100 cP, so the vesicle suspension and the gel network seem to be compatible and the consistency was not changed in any practical way. A viscosity of this order is typical of a firm Carbopol gel. It should hold the preparation in place, while the spreadability of 15.69 g·cm/s indicates that it can still be spread easily over the skin. Spreadability and viscosity pull in opposite directions, and the balance obtained here seems acceptable for topical use (Garg *et al*., 2002).

Table 2: Physical properties of the gel base and the ethosomal gel

Property	Carbopol 934 gel base	Quercetin ethosomal gel
pH	7.3	7.9
Viscosity (cP)	≈ 73,400	≈ 75,100
Spreadability (g·cm/s)	–	15.69

The pH needs some comment. The gel was neutralised to about 7.0 in preparation, but the final ethosomal gel measured 7.9, which is more alkaline than the usual skin surface pH, normally in the mildly acidic range. A pH of 7.3–7.9 is unlikely to be harmful in a short exposure, but for repeated application it would be better to lower it towards 6–6.5 by reducing the amount of neutraliser, and the viscosity would then have to be re-checked because Carbopol gels are sensitive to pH. Quercetin is also less stable at higher pH, which is a further reason to adjust it. We did not test irritation or stability.

3.2 Release and Permeation across Rat Skin

The ethosomal gel delivered more quercetin to the receptor than the plain gel at every sampling time (Table 3, Figure 1). In the first hour, 33.53% of the drug had crossed from the ethosomal gel, against 4.46% from the plain gel. After 24 h the figures were 81.97% and 53.93%, and after 48 h 90.47% and 62.37%. The plain gel released slowly throughout and did not reach 70% in 2 days.

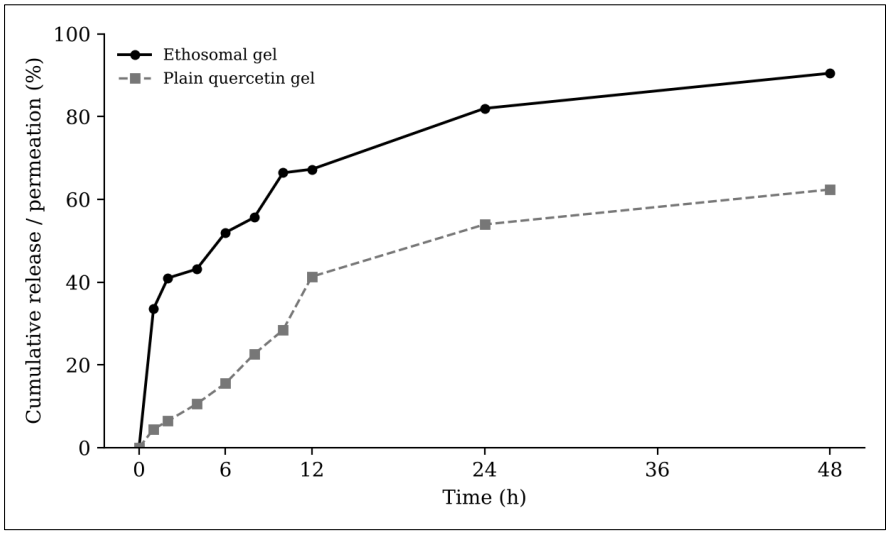


Figure 1: Cumulative release and permeation of quercetin across excised rat skin from the ethosomal gel and from a plain quercetin gel.

Table 3: Cumulative release and permeation of quercetin (%)

Time (h)	Ethosomal gel	Plain quercetin gel
0	0	0
1	33.53	4.46
2	40.98	6.45
4	43.13	10.56
6	51.97	15.54
8	55.62	22.62
10	66.41	28.43
12	67.26	41.32
24	81.97	53.93
48	90.47	62.37

Franz diffusion cell, excised rat skin, receptor phosphate-buffered saline pH 7.4, 37 °C.

Several features of the vesicular system could explain the difference. The drug in ethosomes is in a finely dispersed form that presents a large surface to the skin. Ethanol and the phospholipids are able to fluidise the stratum corneum lipids and carry drug into the skin (Touitou *et al*., 2000; Verma & Fahr, 2004), and the plain gel contains none of these. A crystalline, poorly soluble drug in a simple gel is held back by its own low solubility and by the barrier of the skin. The size of the gap between the two curves is consistent with these ideas, but the experiment does not allow us to separate vehicle effects from vesicle effects, because the plain gel differed from the ethosomal gel in several ways at once.

The profile of the ethosomal gel was not smooth. A third of the drug appeared in the first hour, but only 7.5 percentage points were added in the second hour and 2.2 points between 2 and 4 h, after which the curve rose again. An early burst of this kind is usually attributed to drug that is free in the vehicle or loosely associated with the vesicle surface, and the slower phase to drug that has to leave the vesicles or the gel network. We did not separate free from entrapped drug in the gel, so this is an interpretation. The jumps from one time point to the next also suggest that replicate data would be helpful, since the results are given without standard deviations. A burst may be wanted for a quick onset of action on the skin, but for a sustained effect it would be a drawback.

3.3 Release Kinetics

For the ethosomal gel, the first-order model gave the best fit (R^2 0.955), followed by Higuchi (0.937) and zero order (0.798) (Table 4). A first-order pattern means that the rate depends on the amount of drug still available, and it is common for systems in which a reservoir is depleted. For the plain gel, the Higuchi equation fitted best (0.930), and zero order and first order were poorer (0.816 and 0.887), which fits steady diffusion from a matrix. The first-order and Higuchi values for the ethosomal gel are not far apart, so, with ten time points and no replicates, we would not read too much into the choice between them.

Table 4: Fit of the release data to kinetic models

Model	Ethosomal gel (R^2)	Plain gel (R^2)
Zero order	0.798	0.816
First order	0.955	0.887
Higuchi	0.937	0.930
Korsmeyer–Peppas, R^2 (n)	0.954 (n ≈ 0.23)	0.973 (n ≈ 0.85)

Calculated from the mean values in Table 3, excluding t = 0. Korsmeyer–Peppas fits used the points up to about 60% release (first five points for the ethosomal gel, eight points for the plain gel).

The Korsmeyer–Peppas exponent for the ethosomal gel (about 0.23) is below the Fickian limit for a planar system, which is not a physically meaningful result for diffusion alone. It arises because a large part of the dose appears within the first hour and the curve then flattens, which pushes the slope of log Q against log t down. The number should be read as a sign of the early burst and not as proof of a particular mechanism. The plain gel gave an exponent of about 0.85, which points to anomalous transport, meaning that diffusion and another process such as swelling of the polymer or the skin membrane contribute together.

3.4 What the Results Do and Do Not Show

The results show that, in this skin model, the ethosomal gel moved more quercetin into the receptor than a plain gel over 48 h. They do not show how much of the drug stays in the skin layers, which is what counts for a drug meant to act locally on inflamed or oxidatively stressed skin. For that, the skin should be tape-stripped, or separated into epidermis and dermis, and its drug content assayed at the end of the study. The effect of the vesicles should also be tested against a hydroethanolic solution of quercetin, which separates the contribution of ethanol from that of the vesicles.

4. Limitations

The release and permeation data are mean values only, with no standard deviations or statistical comparison, and the number of replicates is not stated. The skin model used excised rat skin, which is more permeable than human skin. The pH of the final gel (7.9) is above the range usually preferred for the skin. The composition of the plain gel is not fully specified here, and only one ethosomal gel was characterised in detail although six Carbopol levels were prepared. Stability on storage, drug content of the gel, skin irritation and skin retention were not examined. The kinetic analysis rests on ten time points and the Korsmeyer–Peppas exponents on five and eight points.

5. CONCLUSION

Quercetin ethosomes were incorporated into a Carbopol 934 gel without a notable change in consistency, and the gel spread easily. In a Franz cell with excised rat skin, the ethosomal gel delivered clearly more quercetin than a plain gel at all times (90.47% against 62.37% at 48 h), with an early burst

and first-order kinetics. Adjusting the pH, confirming the results with replicates and a hydroethanolic control, and measuring skin retention are the most important steps for taking this formulation further.

DECLARATIONS

Conflict of Interest: None.
Funding: None

REFERENCES

- Barry, B. W. (2001). Novel mechanisms to enable successful transdermal drug delivery. *European Journal of Pharmaceutical Sciences, 14*(2), 101–114.
- Costa, P., & Sousa Lobo, J. M. (2001). Modeling and comparison of dissolution profiles. *European Journal of Pharmaceutical Sciences, 13*(2), 123–133.
- Fathalla, D., Youssef, E. M., & Soliman, G. M. (2020). Liposomal and ethosomal gels for the topical delivery of anthralin: Preparation, comparative evaluation, and clinical assessment in psoriatic patients. *Pharmaceutics, 12*(5), 446.
- Ferrara, F., Benedusi, M., Sguizzato, M., Cortesi, R., Baldisserotto, A., Buzzi, R., Valacchi, G., & Esposito, E. (2022). Ethosomes and transethosomes as cutaneous delivery systems for quercetin: A preliminary study on melanoma cells. *Pharmaceutics, 14*(5), 1038.
- Garg, A., Aggarwal, D., Garg, S., & Singla, A. K. (2002). Spreading of semisolid formulations: An update. *Pharmaceutical Technology, 26*(9), 84–105.
- Godin, B., & Touitou, E. (2004). Ethosomes: New prospects in transdermal delivery. *Critical Reviews in Therapeutic Drug Carrier Systems, 21*(1), 63–102.
- Higuchi, T. (1963). Mechanism of sustained-action medication: Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. *Journal of Pharmaceutical Sciences, 52*(12), 1145–1149.
- Korsmeyer, R. W., Gurny, R., Doelker, E., Buri, P., & Peppas, N. A. (1983). Mechanisms of solute release from porous hydrophilic polymers. *International Journal of Pharmaceutics, 15*(1), 25–35.
- Mbah, C. C., Builders, P. F., & Attama, A. A. (2014). Nanovesicular carriers as alternative drug delivery systems: Ethosomes in focus. *Expert Opinion on Drug Delivery, 11*(1), 45–59.
- Ritger, P. L., & Peppas, N. A. (1987). A simple equation for description of solute release I. Fickian and non-Fickian release from non-swellable devices in the form of slabs, spheres, cylinders or discs. *Journal of Controlled Release, 5*(1), 23–36.
- Touitou, E., Dayan, N., Bergelson, L., Godin, B., & Eliaz, M. (2000). Ethosomes—novel vesicular carriers for enhanced delivery: Characterization and skin penetration properties. *Journal of Controlled Release, 65*(3), 403–418.
- Verma, D. D., & Fahr, A. (2004). Synergistic penetration enhancement effect of ethanol and phospholipids on the topical delivery of cyclosporin A. *Journal of Controlled Release, 97*(1), 55–66.