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FORMULATION AND INVITRO EVALUATION OF TRANSDERMAL PATCH OF QUERCETIN

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ABSTRACT

The purpose of this research is to solve this constraint by designing a transdermal drug delivery system for quercetin that may be administered once daily. This system will provide greater patient compliance, increased bioavailability, and prolonged release compared to other methods.

On the other hand, its therapeutic value is restricted due to difficulties associated with poor solubility, low bioavailability, and unpredictable pharmacokinetics when it is administered orally. For the purpose of determining drug flow and permeation parameters, skin permeation experiments are carried out. This is followed by the use of in vitro or in vivo models for the purpose of evaluating the potential for skin irritation caused by the prepared patches.

The study aims to achieve several objectives: to formulate a transdermal delivery system capable of sustained release of quercetin over 24 hours. A once-daily transdermal delivery system for quercetin that has sustained release properties is one of the outcomes that is anticipated. The formulation included namely dichloromethane and methanol in a ratio of 1:1, using a method called solvent evaporation. Therefore, linseed oil and eugenol were added to the polymer solution in order to improve the penetration. Polyethylene glycol was employed as a plasticizer, and menthol was added in order to counteract the irritation caused by the polymer. Following the preparation of the films in this manner, they attached to the layer of adhesive bandage that had been acquired from the neighbourhood store.

Keywords: Storage conditions, Accelerated aging, adhesive properties, Drug content uniformity, Controlled release.

Abbreviations: TDDS: Transdermal drug delivery system, PVC: Poly Vinyl Chloride

INTRODUCTION

The objective of this research is to improve the therapeutic effectiveness, patient compliance, and safety profile of this powerful flavonoid molecule. Transdermal drug delivery systems represent a significant improvement in pharmaceutical technology, offering a non-invasive approach to delivering therapeutic agents through the skin directly into the bloodstream of the patient. This method bypasses the gastrointestinal tract and hepatic first-pass metabolism, thereby enhancing drug bioavailability and achieving more consistent plasma concentrations over an extended period without supervision of healthcare professional for longer time. These systems have revolutionized the prevention and treatment landscape for conditions ranging from chronic pain management to hormone replacement therapy, underscoring their utility in improving patient quality of life.

Transdermal drug delivery systems (TDDS) for quercetin are intended to administer therapeutic amounts of the substance via the skin and into the systemic circulation. It is the goal of these systems to overcome the physiological barriers that are present in the skin, which include the stratum corneum, epidermis, and dermis, and to enable the effective absorption of drugs while simultaneously limiting the amount of local irritation, systemic adverse effects, and dose frequency.

Polymers, solvents, penetration enhancers, plasticizers, and stabilizers are examples of excipients that are selected for their compatibility with quercetin, skin tolerability, regulatory approval status, and the qualities that are sought in the formulation. Polymers including polyvinylpyrrolidone (PVP), polyethylene glycol (PEG), hydroxypropyl methylcellulose (HPMC), and ethyl cellulose (EC) are often used as matrix materials or film-forming agents for the purpose of controlling the release of drugs and improving their adherence to the skin.

In the process of developing a once-daily TDDS for quercetin, one of the major goals is to improve skin penetration. This is because the stratum corneum is the principal barrier that prevents drugs from being absorbed through the skin. The enhancement of skin permeation may be accomplished by the use of a variety of methodologies, such as physical approaches, chemical enhancers, and alterations to the formulation.

Transdermal drug delivery systems, often known as TDDS, are an advanced method of giving drugs via the skin in order to achieve systemic effects. When compared to the conventional oral or parenteral methods, this approach provides a number of benefits, including as increased patient compliance, less adverse effects, and sustained drug release over a longer length of time.

Topical drug administration is a flexible technique that may be used for the treatment of a wide range of illnesses. It provides targeted therapy, reduces systemic adverse effects, and improves patient compliance. In the fields of dermatology, ophthalmology, and pain management, topical formulations play an essential part in the treatment of a broad variety of problems. These conditions include skin disorders, eye diseases, and musculoskeletal pain, among thousands of others. This article examines the numerous techniques to treating a variety of ailments that make use of topical medication administration.

This research aims to delve into the comprehensive evaluation of transdermal patch stability across different environmental settings. By systematically exploring the effects of varying temperature and humidity conditions on patch integrity and performance, this study seeks to elucidate the underlying mechanisms that govern stability under stress.

In the stability of transdermal patches under diverse storage conditions represents a critical area of investigation within pharmaceutical research. By examining how environmental factors impact patch stability, this study aims to bridge the gap between theoretical formulation and practical application, ultimately advancing our ability to deliver safe, effective, and reliable therapies through innovative transdermal drug delivery systems.

I. LITERATURE REVIEW

Attar, Esha et al., (2023) It has been suggested that quercetin, a flavonoid that occurs naturally, has a broad range of medicinal qualities. On the other hand, the oral administration of quercetin is restricted owing to its low bioavailability, low water solubility, quick metabolism, and rapid plasma clearance as well as its rapid metabolism. There has been a significant amount of research conducted on quercetin when it is combined with a variety of nanodelivery technologies in order to improve its bioavailability. Several different quercetin-loaded nanosystems, including nanosuspensions, polymer nanoparticles, metal nanoparticles, emulsions, liposomes or phytosomes, micelles, solid lipid nanoparticles, and other lipid-based nanoparticles, have been investigated in in-vitro cells, in-vivo animal models, and human subjects. The goal of these studies is to improve the oral bioavailability and effectiveness of the drug. In addition to the nanosystems that have been described, quercetin phytosomes are now available on the market and are gaining a growing amount of attention. Specifically, the current study focuses on anticancer applications and the clinical advantages of nanoquercetin formulations. It also provides insights into the potential of harnessing quercetin for a variety of possible therapeutic applications.

Colino, Clara Isabel et al., (2022). Some have proposed quercetin, a flavonoid, as a treatment or preventive approach for melanoma and other skin diseases due to its powerful antioxidant and anti-inflammatory properties. On the other hand, its formulation is hampered by its poorly soluble and unstable properties. Because of this, the purpose of the current research was to create, analyze, and evaluate lipidic nanoformulations of quercetin that were designed for application in the dermis. Using the hydration method, followed by sonication and extrusion, we created liposomes (F1, F2) and chitosomes (F3, F4) using egg phosphatidylcholine and two different amounts of surfactant (Tween 20). These techniques were followed by the preparation of the liposomes. We assessed the proportion of quercetin that was encapsulated using high- performance liquid chromatography (HPLC), as well as the particle size and zeta potential, the release profile of quercetin, the antioxidant effect, the stability, and the skin accumulation. Liposomes had a zeta potential that was negative, whereas chitosomes had a zeta potential that was positive. The size of the produced vesicles ranged from 184 nm to 342.7 nm. Both of the vesicles had an encapsulation percentage that was more than 78% complete. Quercetin that was encapsulated in vesicles retained its antioxidant activity, which was superior for chitosomes owing to the synergistic effect of chitosan. Chitosomes were thus shown to be superior. The quercetin was released in a regulated manner, as seen by the release profiles. Quercetin may be administered via the dermal route using the formulations that have been produced since they possess the required properties.

Patel, Dhaval et al., (2021) The aim of the present investigation was to develop and evaluate transdermal patch of Apixaban. Formulation development of Apixaban Transdermal patch was initiated using Eudragit S 100 and HPMC E50 LV as matrix controlling polymer for matrix type Transdermal Patch. PEG 400 was selected as plasticizer. Glycerin was selected as permeability enhancer. Preformulation study was performed to check the drug excipient compatibility. The IR spectra of Drug and final formulation found satisfactory. There are no any interaction between drug and excipients. Further the linearity curve was developed in UV for method of analysis. Trials A1-A14 was initiated using different concentration of polymers in the formulation. The prepared patches were transparent and smooth in surface. The weight variation was found well within acceptable range. The thickness of patches was found uniform in nature and the variation is found satisfactory. Further, the surface pH of the patches was found between 6.8 to 7.1 and it is acceptable. The drug content, folding endurance and %elongation results of A1-A14 batches were found well within acceptable range. Initially the trial batches were taken with a single polymer like HPMC and EudragitS100. The drug release was not achieved as per the target drug release profile for 8hours. Hence the combination of these two polymers is taken and found better results than the single polymers. Based on the drug release data, it was observed that the A8 batch was the most satisfactory batch with respect to drug release and other parameters. Hence, the A8 batch selected as optimized batch and Stability study of the same batch initiated.

Sharma, Purnendu et al., (2017) the transdermal patch formulation has many advantages, including noninvasiveness, an ability to bypass the first-pass metabolism, low dosage requirements, and prolonged drug delivery. However, the instability of solid-state drugs is one of the most critical problems observed in transdermal patch products. Therefore, a well-characterized approach for counteracting stability problems in solid-state drugs is crucial for improving the performance of transdermal patch products. This review provides insight into the solid-state stability of drugs associated with transdermal patch products and offers a comprehensive update on the various approaches being used for improving the stability of the active pharmaceutical ingredients currently being used.

Banerjee, Subham et al., (2014) The current study evaluated the stability potential of a transdermal patch composed of eserine and pralidoxime chloride for prophylaxis against (±)-anatoxin A poisoning. The drug combinations were fabricated in an adhesive matrix system supported by a backing membrane and attached to a temporary release liner. Stability testing of the optimized formulation was established for 6 months under accelerated study conditions as per International Conference on Harmonisation guidelines. Results obtained after 6 months showed that the optimized patch formulation was stable with respect to drugs content, pH, diffusion, visual inspection, and other analytical parameters.

Patel, Rakesh et al., (2009) The purpose of this research was to develop a matrix-type transdermal therapeutic system containing drug Aceclofenac with different ratios of hydrophilic (hydroxyl propyl cellulose) and hydrophobic (ethyl cellulose) polymeric systems by the solvent evaporation technique by using 15 % w/w of dibutyl phthalate to the polymer weight, incorporated as plasticizer. Different concentrations of oleic acid and isopropyl myristate were used to enhance the transdermal permeation of Aceclofenac. The physicochemical compatibility of the drug and the polymers studied by differential scanning calorimetry and infrared spectroscopy suggested absence of any incompatibility. Formulated transdermal films were physically evaluated with regard to thickness, weight variation, drug content, flatness, tensile strength, folding endurance, percentage of moisture content and water vapour transmission rate.

II. MATERIALS AND METHODS

COLLECTION, IDENTIFICATION AND AUTHENTICATION OF QUERCETIN:

Quercetin gift sample was collected and received from the kshipra biotech pvt limited, Indore, M.P.

ISOLATION OF QUERCETIN:

The medication was ground into a powder and then extracted from the substance. For the purpose of maceration, fifty grams of raw powder were kept seven days in two hundred milliliters of ethanol. A concentrated extract was obtained by reworking the residue that was left behind. At a lower dry pressure, the extracted substance was filtered, mixed, and concentrated once it had been obtained.

CHARACTERIZATION OF QUERCETIN:

TLC: Activation of the chromatographic plates was place at a temperature of 105 degrees Celsius. For the purpose of reference, the application of quercetin was carried out using the standard medication. Ethyl acetate, toluene, and formic acid are the solvents that are used for the chromatography process. The ratio of these solvents is 4:3. 5: 0.3. Following the drying process in the sun, the chromatographic plates were examined in a UV room.

HPLC: The chromatographic procedures are carried out using the mobile phase consisting of acetonitrile and water at a ratio of 95:5 respectively.

HPTLC: a sample solution with a concentration of one thousand parts per million (ppm) has been prepared. There was a preparation of a Quercetin solution with a concentration of 1000 parts per million. HPTLC conditions that have been optimized.

Spectroscopic studies UV spectroscopy:

The preparation of the sample at a concentration of one thousand milligrams per milliliter by dissolving ethanol and quercetin in the necessary amounts. A similar process is used to make standard solution, which involves dissolving the required strength from stock solution.

Infrared (IR) spectroscopy:

An infrared Fourier transform spectroscopy (FTIR) analysis was performed on the sample after it was generated by combining the separated fraction of quercetin with KBr at a ratio of one hundred to one.

PREFORMULATION STUDIES OF QUERCETIN:

The identification, melting point, solubility tests, partition coefficient, and drug- excipient interaction calculations are all included in this research.

Organoleptic properties: In accordance with the established protocols, the organoleptic qualities were determined.

Melting point: It was determined that a melting point device was used to determine the melting point of the drug sample. The device accommodated both the capillary and the thermometer that had been assembled. When the medication first started to dissolve, the temperature was monitored until the drug had entirely dissolved through the measurement.

Solubility: The quercetin solubility test was carried out by dissolving 5 milligrams of the compound in 5 milliliters of water. Methane: PBS pH 7.4 solvent various solvents to assess solubility in different solvents such as ethanol, methanol, water, PBS (pH 7.2), methanol was used (10: 90), and methanol: PBS pH 7.4 (20: 80). PBS pH 7.4 (05: 95) was the solvent that was employed.

Partition coefficient (PC): The shaking flask technique was used in order to accurately quantify the PC of the quercetin that was separated. For the purpose of this investigation, ten milligrams of the medication were extracted and placed in a vial with a capacity of sixty milliliters. Following this, twenty milliliters of a buffer (phosphate) with a pH of seven and a half were added, and the mixture was agitated. Finally, twenty milliliters of n-octanol were added. Because the n-Octanol layer was higher than the water layer, the octanol layer was lower in density than the water layer. After being agitated for a period of twenty-four hours, the system was then allowed to equilibrate in a separating funnel for thirty- four hours. Following that, the two stages were divided. Consequently, the UV spectrophotometer was used to arrive at an estimate of the medication concentration at 327 nm. Po/w = C organic/C aqueous

Compatibility studies of drugs and excipients: After placing the drug and the excipient in an ampoule at a ratio of one to one, the ampoule was then sealed. According to Saini and Gupta (2009), the sample was physically examined after it had been stored to check for elements such as liquefaction, encrustation, odor or gas, and discoloration.

FORMULATION DEVELOPMENT OF TRANSDERMAL PATCHES:

In the process of formulation development, a casting approach based on solvents is used. One of the components of the matrix type transdermal patch is a polymer that has been meticulously weighed and then combined with appropriate solvents, namely dichloromethane and methanol in a ratio of 1:1, using a

method called solvent evaporation. Therefore, linseed oil and eugenol were added to the polymer solution in order to improve the penetration. Polyethylene glycol was employed as a plasticizer, and menthol was added in order to counteract the irritation caused by the polymer. All of these components were thoroughly mixed using a magnetic stirrer. After dissolving quercetin in the preceding solution, it was put into a petridish that was protected by a funnel and placed in an inverted position. The petridish was then left to evaporate for a period of twenty-four hours. Following that, the patches were enveloped in membrane, cut down to the required dimensions, and then packaged in foil sheets before being stored in dryers. Following the preparation of the films in this manner, they attached to the layer of adhesive bandage that had been acquired from the neighbourhood store.

Preparation of Formulations of Different Transdermal Patches of Quercetin

Different formulations of the Quercetin transdermal patch were prepared as below:

Table 3. 1 Formulations of Quercetin Transdermal Patch:

Formulation	Q1	Q2	Q3	Q4	Q5	Q6
Quercetin(mg)	18	18	18	18	18	18
HPMC(mg)	25	50	75	100	125	150
Ethyl Cellulose(mg)	150	125	100	75	50	25
Eugenol(ml)	0.5	0.5	0.5	0.5	0.5	0.5
Menthol (ml)	5%	5%	5%	5%	5%	5%
Linseed oil (ml)	3%	3%	3%	3%	3%	3%
Poly Ethylene Glycol	3 %	3 %	3 %	3 %	3 %	3 %
Solvent	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

III. EVALUATION OF THE TRANSDERMAL PATCHES:

Physical parameters of different films were determined.

Physical appearance: The color, flexibility, clarity, and softness of each and every transdermal patch that had been already made were evaluated.

Weight variation: The weight of each individual unit of film was determined using a digital scale, and the average weight of the film was used to determine the total weight of the film (Hull M S et al 2002).

Thickness uniformity: Vernier digital calipers were used in order to ascertain the thickness, and the average was computed (Hull M. S., 2002 and Krishnaia Y. S., 2004).

Folding Endurance: Through this test, the sample is evaluated to determine whether or not it is suitable for bending and brittleness. A sharp tool was used to cut through three films comprised of each formulation. As part of the research conducted by Krishnaia Y. S. et al. (2004), the mean value and the standard deviation were computed.

Flatness: Calculating the percentage of shrinkage allowed for the estimation of the length of each individual strip, as well as the measurement of the variance in their measurement. Planarity of one hundred percent is equivalent to the zero percent restriction.

Determination of surface pH: After being cut, the film was stored in distilled water for a period of one hour.

To determine the pH of the surface, a combination glass electrode was placed in close proximity to the surface of the film and allowed to equilibrate for a period of one minute.

In vitro permeation studies: The Franz diffusion cell was used in the in vitro permeation investigation that was carried out. We utilized male rats of the Wistar strain with full skin thickness and an abdominal measurement of 250 grams. An electric cutter that had been equilibrated for one hour in a buffer phosphate solution with a pH of 7.4 was used to gently remove the hair from the abdomen area. Prior to the experiment, the hair was then put on a magnetic stirrer with a tiny magnetic needle in order to ensure that the solution was distributed evenly throughout the body. Using a thermostated heater, the temperature is maintained at 32 degrees Celsius with a margin of error of ± 0.5 degrees Celsius. At predetermined intervals, the volume of the sample, which was 5 milliliters, was extracted from the receptor compartment, and an equivalent amount of new buffer was subsequently reintroduced. After the samples were filtered, a double-beam ultraviolet spectrophotometer was used to conduct the analysis.

Figure 4. 1 Preparation of Medicated Transdermal Patch

IV. RESULTS AND DISCUSSION

Table 5.1 Evaluation parameters of transdermal patch

Code	Weight (mg) ± SD	Thickness (mm) ± SD	Folding endurance ± SD	Flatness (%)	Surface pH
Q1	215.30 ± 2.68	0.331 ± 0.001	304.3 ± 2.52	100	5.43
Q2	212.10 ± 2.48	0.482 ± 0.001	304.6 ± 2.51	100	5.66
Q3	210.70 ± 4.01	0.349 ± 0.001	378.1 ± 2.31	100	5.47
Q4	218.90 ± 2.45	0.453 ± 0.002	302.6 ± 2.08	100	5.67
Q5	214..10 ± 2.77	0.350 ± 0.001	298.3 ± 2.08	100	5.52
Q6	215.80 ± 2.74	0.354 ± 0.001	308.6 ± 2.08	100	5.71

(n = 3), Values are shown as mean SD

Table 5.2 Water vapor absorption(wva) studies of transdermal patch

Code	Initial weight of Patch (mg)	Weight of Patch			Total Moisture Gain	Moisture Absorption %	WVA rate =WL/S
		Day 1	Day 2	Day 3			
Q1	218.43 ± 2.10	218.67	218.89	219.17	0.74 ± 0.006	0.3516 ± 0.003	0.003161
Q2	213.33 ± 1.72	2131.65	213.91	214.23	0.9 ± 0.007	0.4537 ± 0.003	0.003217
Q3	210..26 ± 2.01	210.31	210.56	210.64	0.38 ± 0.003	0.1798 ± 0.001	0.001386
Q4	218.19 ± 2.13	218.57	218.91	219.24	1.05 ± 0.01	0.4282 ± 0.004	0.004349
Q5	214.31 ± 2.10	214.76	214.87	215.09	0.78 ± 0.006	0.3762 ± 0.003	0.002955
Q6	219.11 ± 2.17	219.67	219.81	220.1	0.99 ± 0.008	0.4072 ± 0.003	0.004051

(n = 3),Values are shown as mean SD □

The formulation Q3, which contains HPMC (75 mg) and ethyl cellulose (100 mg), hada much lower level of water absorption than the other formulations.

IN VITRO DRUG RELEASE STUDIES

In vitro drug release studies are critical investigations that are carried out throughout the process of developing and optimizing pharmaceutical formulations. The purpose of these studies is to assess the release kinetics, dissolution behaviour, and drug delivery efficacy in circumstances that are mimicked to be physiological. The objective of theseresearch is to forecast and evaluate the release profile of active pharmaceutical ingredients (APIs) from dosage forms such as tablets, capsules, patches, and implants. The results of these studies will provide useful insights into the processes of drug release, release rates, and formulation characteristics. When it comes to pharmaceutical research, formulation development, quality control, and regulatory filings, in vitro drugrelease studies are very important. These studies help guide the design and optimization of dosage forms that have improved therapeutic effectiveness and patient acceptance.

PREPARATION OF CALIBRATION CURVE OF QUERCETIN

In the field of quantitative analysis, the construction of a calibration curve for quercetinis an essential step, notably in the fields of pharmaceutical, biochemical, and food science research. A link is established between the concentration of quercetin in a sample and the response that it causes in a particular analytical technique, which is oftenspectrophotometry.

A calibration curve for quercetin is prepared using a methodology that consists of manyimportant phases, the first of which is the selection of an acceptable analytical technique. The next step is the creation of standard solutions of quercetin with known concentrations. Ultraviolet-visible spectrophotometry is the method that is used the most often for the purpose of measuring quercetin. This is mostly owing to its high sensitivity, widespread availability, and straightforward operation. The subsequent stage comprises the production of a set of standard solutions that encompass a range of concentrations that bracket the predicted concentration range of the samples that are going to be examined. The preparation of these standard solutions normally involves diluting a stock solution of quercetin, the concentration of which is properly evaluated by the use of gravimetric or volumetric techniques. It is necessary to exercise caution in order to guarantee the consistency and uniformity of the standard solutions, as well as to reduce the number of experimental mistakes that occur during the process of preparation and handling.

When it comes to quercetin, this normally takes place in the ultraviolet area, with absorption maxima occurring at around254 nm (UV-C) or 365 nm (UV-A". On the other hand, the selection of the wavelength might change based on the solvent, the pH of the sample, and the presence of compounds that interfere with the analysis. This necessitates the optimization and validation of the analytical process.

Aliquots of varying concentrations, ranging from 2, 4, 6, 8, and 10 µg/ml, were brought together. At a wavelength of 256 nm, the absorptivity coefficient of the medication wascalculated.

Table 5.3 Calibration of quercetin at 256 nm λmax in methanol

S.No.	Concentration (µg/ml)	Absorbance
1.	0	0
2.	2	0.218
3.	4	0.445
4.	6	0.614
5.	8	0.802
6.	10	0.912

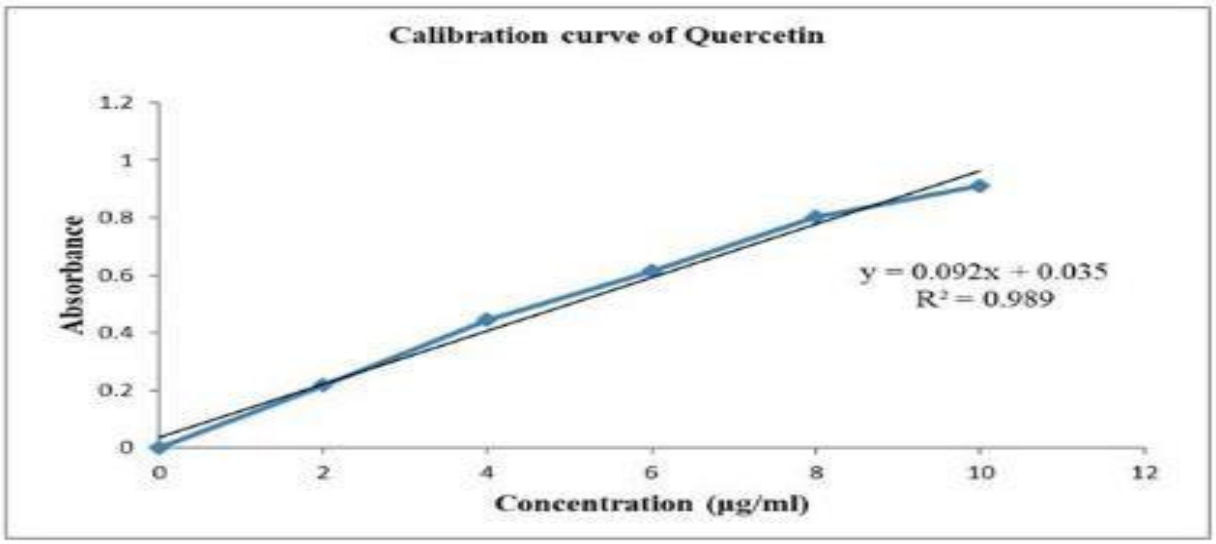

Figure 5.1 Calibration Curve of Quercetin in Methanol

Table 5.4 Absorbance values of quercetin in methanol: pbs ph 7.4 (20: 80)

	Concentration (µg/ml)	Absorbance
1.	0	0
2.	2	0.250
3.	4	0.495
4.	6	0.702
5.	8	0.911
6.	10	0.952

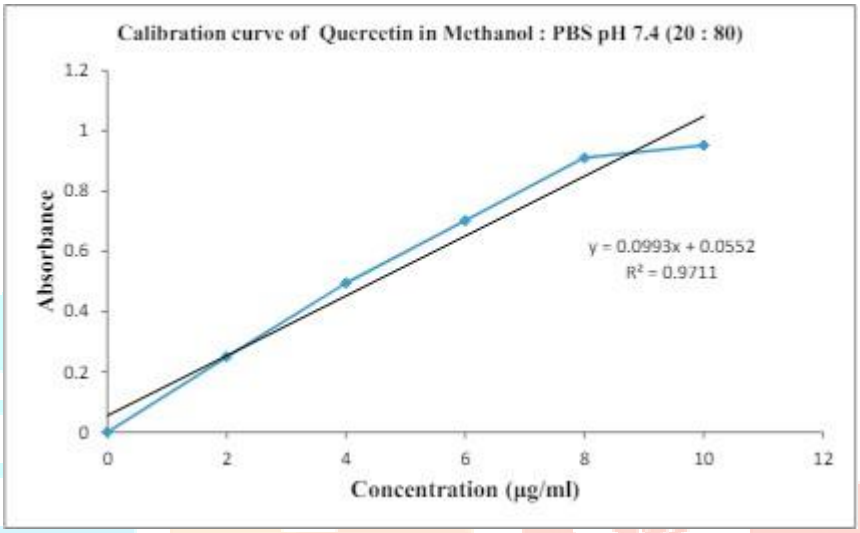

Figure 5.2 Calibration Curve Of Quercetin in Methanol: PBS PH 7.4

CULMULATIVE PERCENTAGE DRUG RELEASE

The drug release rates for the formulations Q1, Q2, Q3, Q4, Q5, and Q6 were found to be 57.02%, 52.66%, 85.77%, 74.78%, 64.27%, and 48.08% at 24 hours, respectively. The sequence of drug release was determined to be Q3>Q4>Q5>Q1>Q2>Q4.

Table 4. 10 Cumulative percentage release of quercetin

The drug release rates for the formulations Q1, Q2, Q3, Q4, Q5, and Q6 were found to be 57.02%, 52.66%, 85.77%, 74.78%, 64.27%, and 48.08% at 24 hours, respectively. The sequence of drug release was determined to be Q3>Q4>Q5>Q1>Q2>Q4.

Table 5.5 Cumulative percentage release of quercetin

CODE	CUMULATIVE % RELEASE OF QUERCETIN										
	1 h	2 h	3 h	4 h	5 h	6 h	7 h	8 h	9 h	10 h	24 h
Q1	0.95	1.81	2.26	5.58	7.24	8.97	9.80	13.50	14.03	15.46	57.02
Q2	0.29	0.44	3.46	5.01	4.04	7.67	8.92	10.40	11.87	13.79	52.66
Q3	4.65	4.20	10.29	12.17	14.45	14.01	18.29	24.50	28.26	30.87	85.77
Q4	2.69	4.01	8.07	9.96	11.66	12.92	14.54	14.60	19.56	21.62	74.78
Q5	1.66	2.57	5.56	7.30	8.88	11.64	12.87	13.86	14.85	17.19	64.27
Q6	2.78	4.21	4.80	4.57	9.2	11.21	12.99	13.92	15.77	17.37	48.08

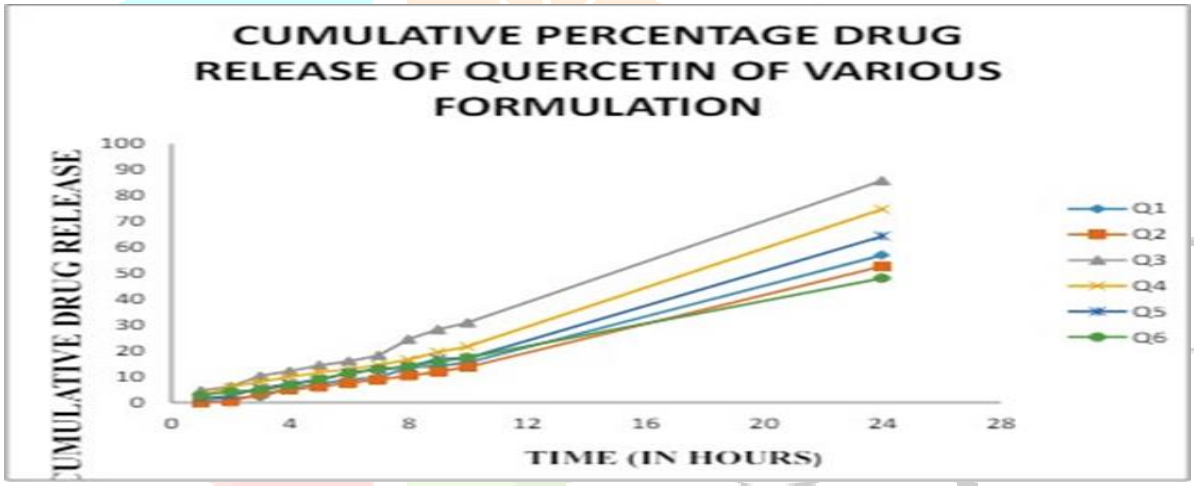

Figure 5.3 Cumulative Percentage Release of Quercetin in Various Formulation

V. CONCLUSION

It may be concluded that the formulation and assessment of quercetin's once-daily transdermal drug delivery constitute a major development in the field of pharmaceuticalresearch and clinical therapies. In the prevention and treatment of a wide range of illnesses and health issues, quercetin, a flavonoid that occurs naturally and has a wide range of pharmacological activities, has shown promising results recently. The therapeutic usefulness of this substance, on the other hand, has been hindered by difficulties associated with its limited bioavailability, poor solubility, and unpredictable pharmacokinetics associated with oral administration. Enhanced bioavailability, prolonged release, and greater patient compliance are all benefits that may be achieved via the creation of a transdermal delivery system for quercetin, which provides a solution to these restrictions.

During the course of this research, it was established that it is possible to achieve sustained medication release over a period of twenty-four hours by using transdermal patches that contain quercetin. The transdermal patches have improved skin penetration and drug flow as a result of the optimization of formulation parameters such as polymer matrix and excipient selection. This ensures that quercetin is delivered via the skin in an effective manner. An understanding of the patches' structural characteristics

and performance has been contributed to by the physicochemical characterization of the patches, which has offered vital insights into the patches' shape, thickness, and moisturecontent.

Through the use of Franz diffusion cells, in vitro release experiments have been conducted to shed insight on the release kinetics of quercetin from transdermal patches. These studies have also highlighted the sustained release profile of these patches and their potential for continuous drug administration. In addition, research on skin permeation have shown that quercetin is capable of diffusing past the barrier that is present on the skin. The parameters of permeation indicate the rate and degree of drug absorption. Following the completion of an evaluation of the risk for skin irritation, thesafety profile of the prepared patches has been validated, therefore assuring that they are compatible with cutaneous application.

Stability testing under expedited and long-term settings has given assurance of the shelf-life and storage stability of the transdermal patches, which is necessary for the economic viability and clinical usage of these patches. Following transdermal delivery, quercetin was shown to have a systemic exposure, which was determined by pharmacokinetic assessment. The pharmacokinetic profile of quercetin was elucidated through the investigation of important parameters such as Cmax, Tmax, and AUC. It has been established that the once-daily transdermal administration of quercetin is therapeutically effective, as indicated by effectiveness evaluation in preclinical models.This highlights the potential of quercetin for the therapy of a variety of illnesses and health problems.

The findings of this study have important repercussions for both the field of research and the therapeutic practice of medicine. The creation of a transdermal delivery system for quercetin that only requires one application per day provides an innovative strategy to improve the delivery of drugs and the effects of therapeutic interventions. Transdermal patches provide benefits over traditional oral delivery, including increased bioavailability and decreased systemic adverse effects. These advantages are achieved by circumventing the hepatic first-pass metabolism and delivering prolonged release. Additionally, the ease of use and patient-friendliness of transdermal distribution are factors that lead to increased treatment adherence and overall patient satisfaction.

The results of this research provide a significant contribution to the expanding body of information about transdermal medication delivery methods and further broaden the range of treatment choices available for quercetin. The further optimization of formulation parameters, the investigation of innovative delivery systems, and clinical assessment in human subjects are all potential future topics for study. In addition, research on the pharmacodynamics and long-term safety profile of transdermal quercetin delivery is required in order to completely clarify the therapeutic potential and clinical value of this method of administration.

The formulation and study of once-daily transdermal drug administration of quercetin constitute a potential step in pharmaceutical research. This method offers a safe, effective, and easy alternative to utilizing the therapeutic effects of Quercetin, which is a naturally occurring molecule. Transdermal delivery systems have the potential to revolutionize medicine delivery and improve patient outcomes across a broad variety of illnesses and health conditions if more research and innovation are committed to developing them.

VI. RECOMMENDATION

Based on the formulation and assessment of once-daily transdermal drug administration of quercetin, numerous suggestions may be made to further optimize the development and implementation of this potential therapeutic strategy. These recommendations include the following:

Optimization of Formulation Parameters: For the purpose of further enhancing the stability, permeability, and release profile of quercetin from transdermal patches, further study should concentrate on fine-tuning the formulation parameters.It is possible to obtain optimum drug delivery performance by doing research on a variety of polymer matrices, penetration enhancers, and excipients using various methods.

Advanced Characterization Techniques: In order to get a more in-depth understanding of the physicochemical characteristics of the transdermal patches, it is necessary to make use of modern

characterisation methods. Detailed information on the morphology, thermal characteristics, and chemical interactions that occur inside the patch matrix may be obtained via the use of techniques such as scanning electron microscopy (SEM), differential scanning calorimetry (DSC), and Fourier- transform infrared spectroscopy (FTIR).

Long-term Stability Studies: It is necessary to carry out rigorous long-term stability tests under a variety of environmental circumstances in order to guarantee the durability and dependability of the transdermal patches throughout the course of time. In order to determine the shelf life and guarantee that the therapeutic effectiveness remains constant during storage and usage, this will be of the utmost importance.

Expanded In Vivo Testing: To further examine the pharmacokinetics, pharmacodynamics, and safety profile of the transdermal quercetin patches, it is necessary to conduct additional in vivo testing in animal models that are relevant to the study. For the purpose of these research, the long-term effects, possible toxicity, and the impact of chronic usage should be evaluated.

Clinical Trials: For the purpose of determining the safety, tolerability, and preliminary effectiveness of the transdermal quercetin patches in human patients, phase I clinical studies should be initiated. In subsequent phase II and phase III studies, the primary emphasis should be on determining the appropriate dosing regimen and comparing the therapeutic results with those of alternative routes of administration.

Patient Compliance Studies: Conduct research to determine whether or if patientsare more likely to comply with the transdermal delivery method and how satisfied they are with it in comparison to oral administration. In order to successfully use this technology in therapeutic settings, it will be essential to first get an understanding of the preferences of patients and then resolve any issues about its usability.

Combination Therapy Exploration: It would be beneficial to investigate the possibility of mixing quercetin transdermal patches with other therapeutic drugs in order to improve the overall effectiveness of the treatment and address more complicated problems. The potential for synergistic effects with other medicationsmight result in treatment techniques that are more all-encompassing.

Regulatory Pathways: During the early stages of the development process, it is important to include regulatory authorities in order to guarantee that the transdermalpatches satisfy all of the relevant regulatory standards. Compliance with Good Manufacturing Practices (GMP), the execution of essential preclinical investigations, and adherence to protocols for clinical trials are all included in this.

Cost-Effectiveness Analysis: It is necessary to do a cost-effectiveness analysis in order to ascertain whether or not the transdermal delivery method is economically feasible. For broad acceptance, it will be essential to take into account the costs of production, the savings that patients would experience as a result of fewer side effects, and greater adherence.

Educational Campaigns: Encourage the development of educational campaigns and materials with the purpose of informing patients and healthcare professionals about the advantages of transdermal quercetin patches and the correct way to apply them. An increase in knowledge and comprehension may make acceptance and incorporation into normal therapy methods easier to accomplish.

Technology Integration: You should investigate the possibility of integrating transdermal patches with intelligent technologies, such as wearable sensors, in order to monitor the release of drugs and the adherence of patients in real time. This has the potential to deliver customized medical techniques and improve the results of therapeutic interventions.

It is possible for researchers and clinicians to progress the development and deployment of once-daily transdermal drug delivery systems for quercetin if they address these suggestions. This will eventually result in an improvement in patient care and an expansion of the therapeutic potential of this natural substance.

VII. REFERENCES

1. Alasdair DT, et al. Pathology Illustrated. II edition, London, Churchill Livingstone; ISBN-10: 0443041679; 1988.
2. Anoop, M.V. and Bindu, A.R., 2015. In-vitro Anti-inflammatory Activity Studies on Syzygiumzeylanicum (L.) DC Leaves. IJPRR, 4(8), 18-27.
3. Bachhav, R.S., Gulecha, V.S. and Upasani, C.D., 2009. Analgesic and anti- inflammatory activity of Argyreiaspeciosa root. Indian journal of pharmacology,41(4), 158.
4. Balasubramanian, A., Ramalingam, K., Krishnan, S. and Ajm, C., 2005. Anti- inflammatory activity of Morusindica Linn. Iranian journal of Pharmacology andTherapeutics, 4(1), 13-0.
5. Chaudhary, B. and Verma, S., 2014. Preparation and evaluation of novel in situ gels containing acyclovir for the treatment of oral herpes simplex virus infections. The Scientific World Journal, 2014. 2014:280928. pp: 1-7.
6. Dhamane, S., 2017. Formulation and Evaluation of Novel Drug Delivery Systemfor Treatment of Peptic Ulcer Ijppr. Human, 9(1), 121-140.
7. Fakhrudin, N., Hastuti, S., Andriani, A., Widyarini, S. and Nurrochmad, A., 2015. Study on the antiinflammatory activity of Artocarpusaltilis leaves extract in mice. Int. J. Pharmacogn. Phytochem. Res, 7, 1080-1085.
8. Gupta, G.D. and Gaud, R.S., 2006. Antiinflammatory activity of tenoxicam gel on carrageenan-induced paw oedema in rats. Indian journal of pharmaceutical sciences, 2006, 68 (3): 356-359
9. Guy, R. H., and Hadgraft, J., ―Selection of drug candidates for transdermal drug delivery in-transdermal drug delivery: developmental issues and researchinitiative‖; Marcel Dekker;Inc. New York.,35, 1989,60-72.
10. Hafeez, A., Jain, U., Sajwan, P., Srivastava, S. and Thakur, A., 2013. Evaluation of Carrageenan induced anti-inflammatory activity of ethanolic extract of bark ofFicusvirens Linn. inswiss albino mice. J Phytopharmacol, 2, 39-43.
11. Hafeez, Abdul & Jain, Upendra & Singh, Jagpal & Maurya, Arun & Rana, Lakhan. (2013). Recent Advances in Transdermal Drug Delivery System(TDDS): An Overview. 733-744.
12. John, N.A.A. and Shobana, G., Anti-inflammatory activity of of Talinum fruticosum on formalin induced paw edema in albino rats, Journal of applied pharmaceutical science, 2012, 2(1), 123.
13. Lashmar U. T., Hadgraft J., Thomas N. Topical application of penetration enhancers to the skin of nude mice; a histopathological study. J. Pharm.Pharmacol. 1989; 41(2), pp 118–122.
14. Lawson AAH, Clinical and pharmacological studies with transdermal Clonidine. In: Prescott LF, Nimmo WS (eds) Rate control in drug therapy. Churchill Living stone, Edinburgh, 1985, pp 215–219.
15. Patel, M., Murugananthan, G. and Gowda, K.P.S., 2012. In vivo animal models in preclinical evaluation of anti-inflammatory activity—A review. Int. J. Pharm.Res. Allied Sci, 1(2), 1-5.
16. Phanse, M.A., Patil, M.J., Abbulu, K., Chaudhari, P.D. and Patel, B., 2012. In- vivo and in-vitro screening of medicinal plants for their anti-inflammatory activity: an overview. J. Appl. Pharm. Sci, 2(6), 19-33.
17. Pharmaceutical Manufacturing Assosiation PMA committee Report: Transdermal drug delivary systems. Pharcop. Forum. 1986, 12, 1798-1807.

18. Sage, B. H., Iontophoresis in Encyclopedia of Pharnaceutical Technology, Vol- 8, Marcel Dekker Inc., New York, 1993, pp217-247.

19. Saini, T.R., Gupta, M.M.,. Preformulation parameters characterization to design, development & formulation of vancomycin hydrochloride tablets for pseudomembrane colitis. International journal of Pharmaceutical research and development. 2009, 1(9), 1-7.

20. Saraf, S., 2010. Applications of novel drug delivery system for herbal formulations. Fitoterapia, 81(7), 680-689.

21. Sharma, Ritu & Basist, Parakh & Alhalmi, Abdulsalam & Khan, Rahmuddin & Noman, Omar & Alahdab, Ahmad. (2023). Synthesis of Quercetin-Loaded SilverNanoparticles and Assessing Their Anti-Bacterial Potential. Micromachines. 14.2154. 10.3390/mi14122154.

22. Sun, Min & Gao, Yan & Pei, Yan & Guo, Chenyu & Li, Houli & Cao, Fengliang& Yu, Aihua & Zhai, Guangxi. (2010). Development of Nanosuspension Formulation for Oral Delivery of Quercetin. Journal of biomedical nanotechnology. 6. 325-32. 10.1166/jbn.2010.1133.

23. Vicentini, Fabiana & Casagrande, Rúbia & Georgetti, Sandra & Vitória, M & Bentley, Maria & Fonseca, Maria & Fonseca, J. (2007). Influence of Vehicle on Antioxidant Activity of Quercetin: A Liquid Crystalline Formulation. LATIN AMERICAN JOURNAL OF PHARMACY. 26. 805-.

24. Wang, Qiang & Hu, Caibiao & Zhang, Hong & Zhang, Yali & Liu, Tian & Qian, Airui & Xia, Qiang. (2016). Evaluation of a new solid non-aqueous self-double- emulsifying drug delivery system for topical application of quercetin. Journal of Microencapsulation. 33. 1-41. 10.1080/02652048.2016.1264494.

25. Zhao, Xingtao & Deng, Ying & Xue, Xinyan & Liao, Li & Zhou, Mengting & Peng, Cheng & Li, Yunxia. (2022). Research Progress of Quercetin Delivery Systems. Current pharmaceutical design. 28