Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 97-106 | ISSN:2251-6727

Creation and Assessment of the Transdermal Patch Containing Extracted CBD and its Anti-Inflammatory Qualities

Jatin Agarwal[*], Dr.Ashok Kumar Rajpoot[1], Dr.Sudhansu, Ranjan Swain[1]

Department Of Pharmaceutics, Moradabad Educational Trust Group of Institution Faculty of Pharmacy, Moradabad, Uttar Pradesh, India.

(Received: 14 April 2024 Revised: 01 May 2024 Accepted: 18 June 2024)

KEYWORDS

Transdermal Patches, Inflammation and Pain, Extracted Cannabidiol Oil, Polymer Matrix, Gaur Gum, Xanthan Gum, Span 80, Glycerin, Solvent Casting method.

ABSTRACT:

Introduction: The transdermal medication delivery system is a unique way to drug administration that overcomes the drawbacks of conventional dosing. The oral route of administration of 74% of medications may not be effective enough. One of the benefits of transdermal medicine administration is that it never causes discomfort. A biological reaction of the immune system, inflammation can be caused on by diseases, wounded cells, and toxic substances. Cannabis plants contain a non-intoxicating substance called CBD..

Objectives: The goal of this project was to create anti-inflammatory transdermal patches that would circumvent metabolism and solve every issue with traditional dosing forms..

Methods: In this study, a transdermal patch containing herbal Extracted medicinal Oil, such as CBD oil, was developed to alleviate inflammation and pain. Polymers and extracted CBD oil were combined to create transdermal patches by the solvent casting technique.

Results: The patches were assessed using physicochemical criteria, including pH, flatness, moisture absorption, drug content, thickness, folding endurance, physical appearance, and weight homogeneity. Additionally, an invitro drug release and stability study was conducted.

Conclusions: In comparison to other formulations, the P5 formulation also has a noticeable effect. Additional in-vitro dissolving research can verify this; the findings supported the notion that the dissolve rate was higher than for other patches.

1. Introduction

Transdermal drug delivery systems (TDDS) have attracted more attention as a means of administering medications via the skin for both systemic and topical distribution, as well as for local therapeutic effects on skin diseases. In comparison to many other drug administration routes, the skin offers a number of important advantages when it comes to drug delivery. These advantages include the ability to avoid issues with gastric irritation, pH, and emptying rate effects; the avoidance of hepatic first-pass metabolism, which increases the drug's bioavailability; the reduction of systemic side effects by minimizing plasma concentrations when compared to oral therapy; and the provision of a sustained release of the drug at the site of application. The decrease in medication changes in plasma levels and the prevention of injection-related discomfort. Additionally, pulsed entrance into the systemic circulation which frequently results in unfavorable side effects can be eliminated by transdermal administration. 1

"Patches" is another term for the transdermal drug delivery system (TDDS). The use of traditional dose forms, such tablets or capsules, has drawbacks, such as low bioavailability due to hepatic first pass metabolism or drug breakdown in the gastrointestinal tract (GIT) via enzyme interactions. Through its potential to inhibit enzymatic or acid-mediated degradation as well as first pass metabolism, TDDSs can improve bioavailability.2 Transdermal distribution of the medication via the epidermis at a regulated rate during the therapeutic

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 97-106 | ISSN:2251-6727

window is an intriguing and patient-compliant new drug delivery technology.3

The skin offers several benefits over other drug delivery methods, including increased patient compliance, reduced gastric irritation, enhanced bioavailability, reduced risk of systemic side effects, sustained drug release, and rapid termination of therapy through reapplication. Thus, TDDS has the potential to reduce adverse effects and increase patient compliance. 4

A painful feeling is a sign that there is an issue in one or more body parts. In general, pain happens whenever bodily tissue is injured, albeit its exact description is unknown.5 all around the body exist afferent pain fibers and pain receptors. Peripheral receptors are the source of the pain feeling when mechanical, thermal, electrical, chemical, etc. stimuli are applied at a threshold high enough to injure tissue. 6 Inflammation is the body's normal reaction to a range of outside agents, including harmful drugs, bodily trauma, and invasive microorganisms. These factors cause the body to retain blood and plasma.7 the body uses inflammation as a natural defense mechanism to get rid of irritating stimuli, but if it is not appropriately handled, it can cause further harm and eventually lead to chronic inflammation. 8

The phytocannabinoid known as cannabidiol (CBD) was identified in 1940. Together with tetrahydrocannabinol (THC), it is one of the 113 known cannabinoids found in cannabis plants. It makes up as much as 40% of the plant's extract. 9 The treatment of anxiety, addiction, psychosis, movement disorders, and pain was the focus of clinical research on CBD as of 2022; however, there is not enough high-quality data to support the effectiveness of cannabidiol for these ailments. 10-13

2. Objectives

Develop and Authenticate Herbal Transdermal patches using Cannabidiol (CBD) Oil for the treatment of Inflammation & Pain. The aim of the study is to prepare and evaluate the Herbal Transdermal patches for the treatment of Inflammation & Pain by using Cannabidiol (CBD) Oil.

3. Methods

Preformulation studies of drug.

Phytochemical screening:

Numerous phytochemical components have been verified to be present in Cannabis sativa L. seeds. In order to preserve their quality, it is crucial to set a standard. To identify the different phytochemical components, the extracts undergo preliminary phytochemical examination. Among the other substances found in the study were alkaloids, glycosides, flavonoids, and tannins.

Determination of UV absorption maxima (λ max):

The identification of drug was done by UV spectrophotometric method. From the spectra, λ max Cannabidiol was observed at 210 nm. The spectral data from this scan was used for the preparation of a calibration curve of Cannabidiol.

Construction Of Standard Calibration Curve Of Cbd: Construction Of Standard Calibration Curve Of Cannabidiol Methanol

The calibration curve is obtained by dissolving 100 mg of CBD in 100 ml of methanol to give 1000 µg/ml this was stock-I solution. From the above,1 ml solution was taken and made up to 10 ml with methanol to give 100 µg/ml this was stock- II. From stock-II 2, 4, 6, 8 ml was taken and made up to 10ml with methanol this gave concentration 2, 4, 6, 8 ,10 µg/ml. Absorbance was measured spectrophotometric ally at 209nm against methanol as blank.

Determination of solubility:

The solubility analysis for Cannabidiol was done by solubility determination in different solvents like Water, Chloroform, Acetonitrile, Ethanol, Methanol, etc.

Development Of Transdermal Patch: [21]

Solvent casting evaporation technique:

The patches were developed by solvent casting evaporation technique. A weighed amount of polymer was mixed in a calculated quantity of Distilled Water and then heated on hot plate. The calculated amount of Drug was added to the polymer solution and thoroughly mixed until the mixture became homogeneous using magnetic stirrer. After the permeation enhancer and glycerin were then added in the calculated amounts. The

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 97-106 | ISSN:2251-6727

resulting solution was put into a petridish and air dried for 24 hours at room temperature. The patches from the petridish were then removed with a knife and then stored in a desiccator. All formulation batches are given in Table 1

. **Table No-3:** Composition of transdermal patches:

F. c	Drug (mg)	Gg (mg)	Xg (mg)	Span 80(ml)	Glycerin (ml)	Water/Methanol (ml)
P1	40	70	70	1	3	20
P2	40	100	70	1	3	20
P3	40	70	100	1	3	20
P4	40	100	100	1	3	20
P5	40	70	85	0.5	3	20
P6	40	100	85	0.5	3	20
P7	40	70	85	1.5	3	20
P8	40	100	85	1.5	3	20
P9	40	85	70	0.5	3	20
P10	40	85	100	0.5	3	20
P11	40	85	70	1.5	3	20
P12	40	85	100	1.5	3	20
P13	40	85	85	1	3	20

1ml=20mg of CBD [36]

Figure 5: Preparation of Casting Solution on Magnetic Stirrer

Figure 6: Casting Solution Is Poured In a Petridish

Evaluation Parameters of Transdermal Patch:

The physical and mechanical characteristics, as well as the permeability of the medicines, are significantly impacted by the transdermal films' composition and

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 97-106 | ISSN:2251-6727

concentration. Medicated transdermal films' mechanical and physical characteristics, including their elasticity modules, tensile strength, moisture absorption, percent flatness, and percent elongation at break, were examined. In vitro drug release, drug content, and area were also assessed for medicated films.

I. Organoleptic Characteristics:

A. Visual appearance:

The Appearance, color, Clarity, Smoothness, and flexibility of the TDDS were assessed visually. 22

II. Physico-Chemical Evaluation:

A. Folding endurance:

A certain 2x2 cm section of the strip was cut consistently, and then folded repeatedly until it broke. The amount of times the film was folded at the same spot—either to break the film or to cause visible cracks—was what determined the folding endurance rating. 23, 24

B. Thickness:

Using a screw gauge and least count at five distinct locations, the thickness of the produced transdermal films was determined. An SD was used to compute the average. 25

C. Weight variation:

The average weight was determined by weighing each of the ten patches from each formulation separately. A substantial deviation from the average weight is not acceptable for any individual. 26

D. Drug Content:

A transdermal patch measuring 2 by 2 centimeters was dissolved in 100 milliliters of methanol and vigorously shaken for a whole day. After that, the entire solution was ultrasonically treated for fifteen minutes. Following filtering, spectrophotometry at 210 nm was used to determine the drug's concentration. 27

$$Drug\ Content\ \% = Absorbance\ of\ test\ / absorbance\ of\ standard\ X\ 100$$

E. Percentage moisture content:

The produced films were weighed one at a time and stored for twenty-four hours at room temperature in a desiccator filled with fused calcium chloride. Following a 24-hour period, the films were weighed again, and the % moisture content was calculated using the formula below:

$$Percentage\ moisture\ content = [(Initial\ weight - Final\ weight)/Final\ weight] \times 100.$$

F. Percentage Moisture Uptake:

To maintain an 84% relative humidity, the weighted films were stored in a desiccator with a saturated potassium chloride solution for 24 hours at room temperature. The films were reweighed after a 24-hour period, and the % moisture absorption was calculated using the formula below: 28

$$Percentage\ moisture\ uptake = [(Final\ weight - Initial\ weight)/Initial\ weight] \times 100.$$

G. Tensile strength:

The polymeric patch was pulled using a pulley system to measure the elongation as a tensile strength. Weights were progressively added to the pan to increase the pulling force until the patch broke. Using a magnifying glass and graph paper, the elongation—that is, the distance the pointer moved before the patch broke—was measured. The tensile strength was computed as kg cm-2. 30

Tensile Strength= Break Force/ a.b (1+ ΔL/L)

Where; a = width of the patch, b = thickness of the patch, L = length of the patch, ΔL = elongation of patch at break point, Break Force= weight required to break the patch (Kg).

H. Flatness:

From each film, three longitudinal strips were removed: one from the left side, one from the right side, and one from the middle. Every strip's length was measured, and the percentage of constriction (0% constriction = 100% flatness) was used to calculate the length variation resulting from non-uniformity in flatness. 31

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 97-106 | ISSN:2251-6727

III. In-vitro drug dissolution study:

Paddle over disk was the approach used for in vitro drug release experiments. Dry films of defined thicknesses were weighed, sliced into circles, and adhered to a glass plate using an adhesive. After that, the plate was submerged in 500 milliliters of phosphate buffer (pH 7.4), and the device was adjusted to 32 ± 0.5 degrees Celsius. After that, the paddle was adjusted to be 2.5 cm away from the glass plate and run at 50 rpm. Samples (5 mL aliquots) were taken out at predetermined intervals for up to 12 hours, and a double beam UV-visible spectrophotometer was used to measure the amount of drug present at 210 nm. Three duplicates of the experiment were run, and the mean value was computed. 29

4. Results

Phytochemical screening

Preliminary phytochemical analysis of Cannabis sativa L Seeds extract

Table 5: Phytochemical screening of plant extracts

PHYTOCHEMICAL	QUALITY	COLOR	TEST
Alkaloid	+ + +	Orange	Dragendoff's
Saponin	-		
Flavonoids	+ +	Light Yellow	Lead acetate
Tannins	-		
Cardiac Glycosides	+ + +	Reddish Brown	Keller-Killani
Balsam	-		
Phenols	-		
Terpenes & Steroids	+ + +	Reddish Brown	Bur chard
Resins	+ + +	Violet	
Volatile Oils	-		

+++High presence ++ moderate presence – Absence

Determination of UV absorption maxima (λ max):

The identification of drug was done by UV spectrophotometric method. From the spectra, λ max Cannabidiol was observed at 210 nm. The spectral data from this scan was used for the preparation of a calibration curve of Cannabidiol.

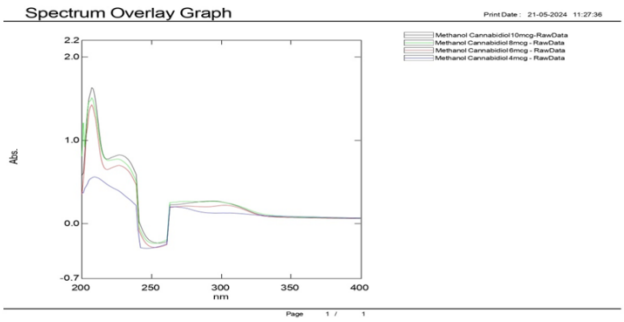

Fig 8: UV ABSORPTION MAXIMA (λ max) of CBD extract

Construction of Standard Calibration Curve of Cannabidiol

The calibration curve is obtained by dissolving 100 mg of CBD extract in 100 ml of methanol to give 1000 µg/ml this was stock-I solution. From the above,1 ml solution was taken and made up to 10 ml with methanol to give 100 µg/ml this was stock- II. From stock-II 2, 4, 6, 8 ml was taken and made up to 10ml with methanol this gave concentration 2, 4, 6, 8 ,10 µg/ml. Absorbance was measured spectrophotometric ally at 210nm against methanol as blank.

Table 6: Construction of Standard Calibration Curve of Cannabidiol extract

S.No	Concentration of Cannabidiol extract	Absorbance at 210 nm
1	2 µg/ml	0.206
2	4 µg/ml	0.507
3	6 µg/ml	0.839
4	8 µg/ml	1.138
5	10 µg/ml	1.428

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 97-106 | ISSN:2251-6727

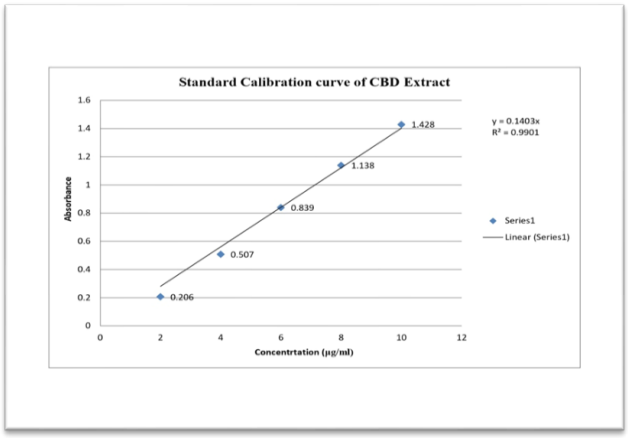

Fig 9: Calibration Curve of Cannabidiol extract

Development of transdermal patch:

Transdermal patches of Cannabidiol extract were successfully developed using the solvent casting evaporation technique. The developed film was homogeneous, flexible, smooth, and clear.

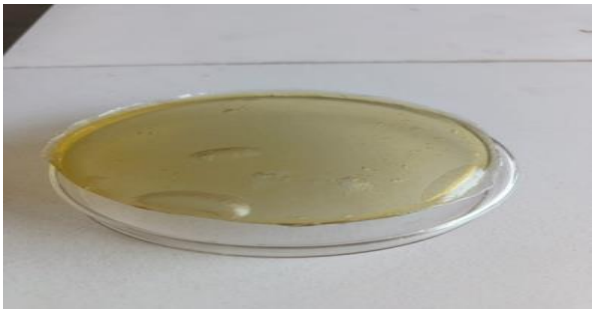

Figure 10: Developed of transdermal patch

Evaluation of Herbal transdermal patches:

Organoleptic Characteristics

Table 7: Organoleptic Characteristics of Herbal Transdermal patches

S. No	Formulation	Appearance	Color	Smoothness	Flexibility
1	P1	Uniformed Preparation	Light yellowish green	Smooth	Flexible
2	P2	Uniformed Preparation	Light yellowish green	Smooth	Flexible
3	P3	Uniformed Preparation	Light yellowish green	Smooth	Flexible
4	P4	Uniformed Preparation	Light yellowish green	Smooth	Flexible
5	P5	Uniformed Preparation	Light yellowish green	Smooth	Flexible
6	P6	Uniformed Preparation	Dark yellowish green	Smooth	Flexible
7	P7	Uniformed Preparation	Light yellowish green	Smooth	Flexible
8	P8	Uniformed Preparation	Dark yellowish green	Smooth	Flexible
9	P9	Uniformed Prepa	Light yellowish	Smooth	Flexible

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 97-106 | ISSN:2251-6727

		ration	**green**		
10	**P10**	**Uniformed Preparation**	**Dark yellowish green**	**Smooth**	**Flexible**
11	**P11**	**Uniformed Preparation**	**Light yellowish green**	**Smooth**	**Flexible**
12	**P12**	**Uniformed Preparation**	**Dark yellowish green**	**Smooth**	**Flexible**
13	**P13**	**Uniformed Preparation**	**Light yellowish green**	**Smooth**	**Flexible**

Physiochemical Evaluation:

Table 8: Physiochemical evaluation of herbal transdermal patches

Formulation	**Folding Endurance**	**Thickness (mm)**	**Weight Variation (mg)**	**% Moisture content**
P1	**100±2.26**	**0.23 ±0.01**	**335 ±3.39**	**6.94 ±1.95**
P2	**94.33±5.8**	**0.18 ±0.02**	**496 ±8.64**	**2.24 ±0.8**
P3	**100±1.13**	**0.22 ±0.02**	**461 ±9.88**	**3.81 ±0.47**
P4	**101±1.13**	**0.18 ±0.02**	**545 ±19.08**	**2.78 ±0.9**
P5	**102±1.72**	**0.24 ±0.01**	**400 ±11.31**	**5.06±1.73**
P6	**86±1.32**	**0.21 ±0.03**	**458 ±4.71**	**3.61 ±0.72**
P7	**87±1.72**	**0.19 ±0.03**	**396 ±11.48**	**3.93 ±0.58**
P8	**98±2.35**	**0.21 ±0.01**	**599 ±10.51**	**2.27 ±0.46**
P9	**83±3.97**	**0.24 ±0.02**	**432 ±8.98**	**4.84 ±1.02**
P10	**90±1.13**	**0.23 ±0.02**	**502 ±8.98**	**2.44 ±0.42**
P11	**93±2.26**	**0.22 ±0.02**	**400 ±14.76**	**3.34 ±0.98**
P12	**92±2.35**	**0.23 ±0.02**	**480 ±17.32**	**2.77 ±0.26**
P13	**87±2.35**	**0.23 ±0.02**	**502 ±4.08**	**2.79 ±0.51**

Table 9: Physiochemical evaluation of herbal transdermal patches

Formulation	% Drug content	% Moisture uptake	Tensile strength(kg/cm^2) (mean ± S.D.)	Flatness
P1	98.54±0.92	6 ±0.49	0.26±0.04	100%
P2	95.79±1.48	4.5 ±1.07	0.32±0.07	100%
P3	83.17±0.70	4.26 ±1.26	0.37±0.05	100%
P4	98.7 ±0.84	3.5 ±1.176	0.49±0.03	100%
P5	88.18 0.63	5.38 ±0.82	0.37±0.09	100%
P6	94.33±0	4.06	0.29 ±0.08	100%

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 97-106 | ISSN:2251-6727

	.84	±1.52		
P7	81.87±1.93	4.56 ±0.80	0.34 ±0.05	100%
P8	89.31±1.98	2.9 ±0.40	0.51 ±0.06	100%
P9	95.63±0.92	3.62 ±1.11	0.45 ±0.06	100%
P10	76.21±0.92	3.73 ±0.39	0.36 ±0.06	100%
P11	85.32±0.79	5.23 ±1.64	0.54±0.02	100%
P12	75.23±1.01	3.53±0.34	0.33 ±0.05	100%
P13	98.21±0.70	4.21 ±0.60	0.27 ±0.03	100%

In-vitro DRUG DISSOLUTION STUDY:

Table 10: In-vitro DRUG DISSOLUTION STUDY

Time in mins	**PERCENTAGE CUMULATIVE RELEASE (%)**												
	P1	**P2**	**P3**	**P4**	**P5**	**P6**	**P7**	**P8**	**P9**	**P10**	**P11**	**P12**	**P13**
0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	2.85	3.2	4.15	5.7	7.35	6.75	5.45	3.85	7.05	8	5.1	2.25	5.78
60	8.35	8.35	10.6	14.1	16.67	17	16.7	10.6	18.6	18	14.45	9.3	17.65
90	18.6	19.6	19.9	25.05	28.25	29.5	32.1	23.1	34.05	32.1	27.95	21.5	33.4
120	39.5	38.55	35.35	41.75	50	52.35	57.2	45	59.45	53	53	48.5	58.8
150	81.95	69.1	68.1	80.35	92.85	93.85	94.15	80.03	99.6	90.6	85.8	85.15	97.05

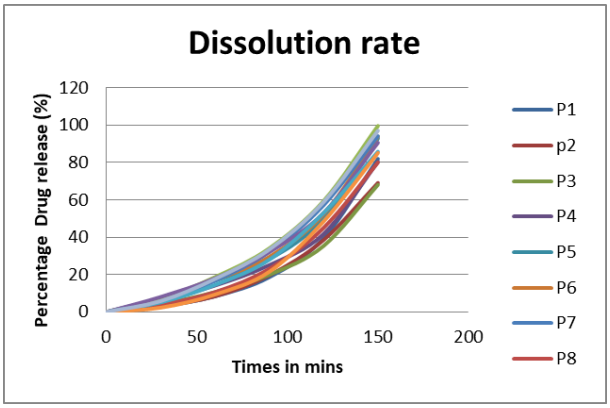

Fig 11: In-vitro DRUG DISSOLUTION STUDY

5. Discussion

Transdermal medication delivery systems are among the most promising approaches of drug delivery. Glycerin, Xanthan gum, and gaur gum were used to make the herbal transdermal patch with extracted cannabidiol oil. After thirteen patches were made, their physical and dissolving characteristics were assessed.

The visual appearance, weight fluctuation, thickness, folding durability, moisture content, drug content, and dissolving study of formulations P1–P13 were among the evaluation criteria that were determined to be good. According to the assessment studies, the patch formulation P5 is superior to the other formulations in terms of uniformity of weight, high folding durability, low moisture content, and less thickness. They also include more medication than other formulations at the same time.

In comparison to other formulations, the P5 formulation also has a noticeable effect. Additional in-vitro dissolving research can verify this; the findings

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 97-106 | ISSN:2251-6727

supported the notion that the dissolve rate was higher than for other patches.

Refrences

1. K. C. Garala, A. J. Shinde, and P. H. Shah, “Formulation and in-vitro characterization of monolithic matrix transdermal systems using HPMC/Eudragit S 100 polymer blends,” International Journal of Pharmacy and Pharmaceutical Sciences, vol.1, no. 1, pp. 108–120, 2009.
2. Wokovich AM, Prodduturi S, Doub WH, Hussain AS, Buhse LF. Transdermal drug delivery system (TDDS) adhesion as a critical safety, efficacy and quality attribute. Eur J Pharm Biopharm 2006;64:1-8.
3. Shivakumar HN, Murthy SN. Topical and transdermal drug delivery. In: Kulkarni VS, editor. Handbook on Non-invasive Drug Delivery Systems. USA: Elsevier Inc.; 2010. p. 1-36.
4. Garala KC, Shinde AJ, Shah PH. Formulation and in-vitro characterization of monolithic matrix transdermal systems using HPMC/Eudragit S 100 polymer blends. Int J Pharm Pharm Sci. 2009;1(1):108–20.
5. Michel YB, Dubois, Christopher G, Allen HL. Chronic pain management. In: Healy TEJ, Knight PR, editors. Wylie and Churchil-Davidson’s A practice of Anaesthesia, 7th ed. London: Hodder Arnold; 2003. p. 1235-9.
6. Guyton C, Hall JE. Medical Physiology, 11th ed. ChurchillLivingstone 2006;598-609.
7. Sobotar R, Szwed M, Kasza A, Bugno M, Kordula T.Parthenolide inhibits activation of signa transducers and activators of transcription (STATS) induced by cytokines of the IL-6 family. Biochem Biophys Res Commun 2000;267:329 33.
8. Coulter A. The signifi cance of pain and infl ammation. Wholistic Health Care. Capital Technologies 2013.
9. Campos AC, Moreira FA, Gomes FV, Del Bel EA, Guimarães FS (December 2012). "Multiple mechanisms involved in the large-spectrum therapeutic potential of cannabidiol in psychiatric disorders". Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences (Review). 367 (1607): 3364–3378. doi:10.1098/rstb.2011.0389. PMC 3481531. PMID 23108553.
10. Kirkland AE, Fadus MC, Gruber SA, Gray KM, Wilens TE, Squeglia LM (February 2022). "A scoping review of the use of cannabidiol in psychiatric disorders". Psychiatry Research. 308: 114347. doi:10.1016/j.psychres.2021.114347. PMC 8799523. PMID 34952255.
11. Black N, Stockings E, Campbell G, Tran LT, Zagic D, Hall WD, et al. (December 2019). "Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis". The Lancet. Psychiatry. 6 (12): 995–1010. doi:10.1016/S2215-0366(19)30401-8. PMC 6949116. PMID 31672337.
12. VanDolah HJ, Bauer BA, Mauck KF (September 2019). "Clinicians' Guide to Cannabidiol and Hemp Oils". Mayo Clinic Proceedings. 94 (9): 1840–1851. doi:10.1016/j.mayocp.2019.01.003. PMID 31447137.
13. Prud'homme M, Cata R, Jutras-Aswad D (January 2015). "Cannabidiol as an Intervention for Addictive Behaviors: A Systematic Review of the Evidence". Substance Abuse. 9: 33–38. doi:10.4137/SART.S25081. PMC 4444130. PMID 26056464.
14. Ansel.H.C, Loyd.A.V, Popovich.N.G, Pharmaceutical dosage forms and drug delivery systems, Transdermal drug delivery system introduction. Lippincott Williams and Willkins publication. Seventh edition, Section 8: pp. 646-668.
15. Peddapalli H, Ganta RP, Boggula N. Formulation and evaluation of transdermal patches for antianxiety drug. Asian J Pharm 2018;12:127
16. Keleb E, Sharma RK, Mosa EB, Aljahwi A-AZ. Transdermal drug delivery system-design and evaluation. Int J Adv Pharm Sci 2010;1:201–11.
17. Bangale GS, Rathinaraj BS, Rajesh KS, Shinde GV, Umalkar DG, Rajveer CH, et al. Design and evaluation of transdermal films of atenolol. J Chem Pharm Res 2010;2:593–604.
18. Pandit V, Khanum A, Bhaskaran S, Banu V. Formulation and evaluation of transdermal films for the treatment of overactive bladder. Int J Pharm Tech Res 2009;1:799-804.

19. El-Gendy. Transdermal delivery of Salbutamol sulphate: Formulation and evaluation. Pharm Dev Technol. 2009;14(2):216–25.
20. Garala KC, Shinde AJ, Shah PH. Formulation and in vitrocharacterization of monolithic matrix transdermal systems using HPMC/Eudragit S 100 polymer blends. Int J Pharm Pharm Sci 2009;1:108–20.
21. E. Keleb, R. Sharma, E. B. Mosa, and A. Z. Zaljahwi, "Transdermal drug delivery system-design and evaluation,"International Journal of Advances in Pharmaceutical Sciences,vol. 1, pp. 201–211, 2010.
22. Anil Reddy B. In vitro characterzatioan and evaluation of transdermal drug delivery system for metoprolol tartarate. J Pharm Res HealthCare 2010;2:325-9.
23. Gupta R, Mukherjee B. Development and in-vitro evaluation of diltiazem hydrochloride transdermal patches based on povidone-ethyl cellulose matrices. Drug Dev Ind Pharm. 2003; 29:1 – 7.
24. Arora P, Mukherjee P. Design, development, physicochemical, and invitro and in-vivo evaluation of transdermal patches containing diclofenac diethylammonium salt. J Pharm Sci. 2002; 91: 2076-2089.
25. https://www.canatura.com/a/cbd-dose-calculation-how-to-do-it#:~:text=The%20answer%20is%2020%20mg,usually%20equals%20one%20full%20dropper