IOSR Journal Of Pharmacy And Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 14, Issue 6 Ser. II (Nov –Dec 2019), PP 26-36
www.Iosrjournals.Org

Formulation and Characterization of Etoricoxib Olive Oil Emulgel by Using Different Gelling Agents

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Abstract: *In present time emulgel is new plateform for drug delievery system because it is useful for hydrophobic drugs. Currently emulsified gels have been growing faster in pharmaceutical topical dosage forms as well as another topical semisolid dosage form. Etoricoxib , a non-steroidal anti-inflammatory drug, has been used in the treatment of joint pain, inflammation, arthritis. Etoricoxib reduces pain and inflammation by blocking COX2, enzyme in the body. This study was conducted to comparison study of parameters of marketed etoricoxib emulgel formulation. The purpose of this study is to evaluate the safety and effectiveness of a new experimental medication for the treatment of moderate to severe joint pain and inflammation. For fulfilling this approach, we are preparting emulgel from Etoricoxib and oil phase of olive oil in emulsion. Because the delivery of the hydrophobic drugs are not possible by simple hydro gel that is only possible by formulating emulgel (emulsion + gel). On the other hand oil phase of olive oil contain oleocanthal, which prevents the production of pro-inflammatory COX-1 and COX-2 similar to classical nonsteroidal anti-inflammatory drugs, which is same as etoricoxib, a synthetic, nonsteroidal anti-inflammatory drug (NSAID) with anti inflammatory activity. To prepared formulation was to undergone various preliminary evaluation like Appearance, pH of gel, drug content, rheological study, spread ability, Extudability. To this study was to concluding that out of six formulation F2 formulation showed the effective result of % drug release and the emulgel of etoricoxib was successfully formulate and evaluate found to be compatible topically.*
Key words:- *Etoricoxib, gelling agents, topical drug delivery system, carbopol.*

Date of Submission: 18-11-2019 Date of Acceptance: 04-12-2019

I. Introduction

TDDS can be defined as a most reliable method for the delivery of drugs through skin. It can easily reaches to the organ of human body for giving therapeutic effects and to cure disorders. Or TDDS is accepted as most secure, important, favorable and reliable substitute to the oral and parenteral drug delivery system because skin act as suitable medium system for drug [1].

In other way we can say that , Topical drug delivery system encourage the skin for obtaining drug during the application of drug to the skin [2]. This method is very use full because topical drug delivery system is most reliable method and act as a alternative of oral route.[3,4] Topical route of drug administration is referred to localized drug delivery system anywhere in restricted area in body through skin, vaginal, rectal etc. skin act as a most reliable and comfort route for topical drug administration. Topical administration is the preferential way to get the effect of drug and cure the disease [5].

Topical medicines are included semisolid dosage form for example

- Patches
- Gels & emulgels
- Ointments
- Creams
- Nanoparticles
- Microemulgel
- Lotion etc.

Eye or Ear :

- Solution
- Suspension
- Ointment

Nose :

- Sprays and powder.

Commonly emulgel is the beneficial medium for those drugs which are not soluble in water means they are hydrophobic drugs. NSAIDs (Nonsteroidal anti-inflammatory agents), antifungal, antiviral drugs can be given in the form of topical semisolid dosage forms, Which include the emulgel dosage form specially in the case of when they consist hydrophobic drugs [6, 7].

Topical drug delivery system's advantages: topical drug delivery system have following advantages. [9, 10, 18]

1. Topical drug delivery system keep away drug from first pass metabolism.
2. Avoid the possibility and difficulty during intravenous therapy.
3. Act as a most reliable alternative for oral route when oral route is incompatible with patient.
4. Easy to apply at restricted area.
5. Easy to handle and carry.
6. Ignore the gastro-intestinal inappropriateness.
7. Increases the bioavailability of drugs .
8. Provide utilization of drugs with narrow therapeutic window.

Topical drug delivery system's disadvantages: Topical drug delivery system have following disadvantages [10,18].

1. Some drugs are poorly permeable to the skin.
2. Skin cannot absorbed the drug with large partical size.
3. Sometimes it causes skin irritation.
4. Carrying with long time it cause difficulties.
5. Possibility of skin irritation(inflammation).

Factors which affect topical absorption of drug: [12, 13, .25]

(A) Physiological Factors

1. Skin thickness.
2. Lipid content.
3. Density of hair follicles.
4. Density of sweat glands.
5. Skin pH.
6. Blood flow.
7. Hydration of skin.
8. Irritation of skin.

(B) Physiochemical Factors

1. Partition coefficient.
2. Molecular weight (<400Dalton).
3. Degree of ionization
4. Effect of vehicles

EMULGEL: [14, 22, 23]

In present time emulgel is new plateform for drug delievery system because it is useful for hydrophobic drugs. Currently emulsified gels have been growing faster in pharmaceutical topical dosage forms as well as another topical semisolid dosage form[15,22,].

Emulgel are refer to the mixture of gelling agent with emulsion where firstly gelling agent was prepared by the soaking overnight gel into water & than emulsion was prepared which can be o/w or w/o emulsion and finally they were mixed togetherand performed emulgel. Hydrophobic drug takes huge advantages from the approaches of emulgel. [16]

The occurrence of water in gelling agent change a classical emulsion into an emulgel. Emulsified gel on behalf of dermatological use have numerous favorable properties for example: [17,18]

- Good Spreadibility Property
- Easy To Applicable ,
- Easily Removable,
- High Bioavailability,
- Clear & Pleasant Appearance Etc. (20 , 21)

In the mid-1980's, Emulsion-gels have been increasing their importance and popularity in both pharmaceutical and cosmetics topical semisolid dosage form as a direct effect of drug including medication to the skin to get the effect of drug or treatment of disorders [22]. Emulsion is a controlled release system surrounded by biphasic liquid dosage form, means two immiscible liquid phases usually consist of organic solvent (oil) & aqueous phase (water), where drug particles of hydrophobic drugs are mixed into oil phase of emulsion which defeat the limitation water base hydrogels and then pass into the aqueous phase pass which give the new plateform gor hydrophobic drugs which is gradually absorbed by skin. Emulgel is secure one and favorable form of topical medication because individually gel & emulsion have some disadvantages [23]. For example major disadvantages of gel has delivery of hydrophobic or poorly water soluble drug which is not possible by simple gel or hydrogel. Because hydrophobic drugs cannot dissolve in gel base, where gel base is water[24,25]. To overcome this limitation emulsified gel (emulgel) provide hydrophobic drug to be mixed into an oil phase which result in o/w emulsion, where oil globule are dispersed in aq. Phase. After that emulgel can be easily prepared by mixing emulsion in gel base. This can be substitute for oral therapy when oral route consist incompatibility. [25, 45, 48]

Fig no 1 : Important roll of gelling agent during preparation of emulgel

Emulgel's advantages: [26,47,61]

1. **Reliable plateform for Delivery of hydrophobic drugs:** emulgel avoide the problem of soulbilty, when most of water insoluble drug (hydrophobic drug) cannot dissolve in gel base, where gel base is water[28]. To overcome this limitation emulsified gel (emulgel) provide hydrophobic drug to be mixed into an oil phase which result in o/w emulsion, where oil globule are dispersed in aq. Phase. After that emulgel can be easily prepared by mixing emulsion in gel base. This can be substitute for oral therapy when oral route consist incompatibility. [29,30]
2. **Emulgel have Better loading capacity:** emulgel showes better loading ability than liposomes and niosomes because niosomes & liposomes have nano size due to small arrangement of cell (small or vesicular structures) possibly will result in leakage of effects or efficiency. [31,36, 55]
3. **Emulgel have Better stability:** further transdermal preparations such as emulsion, powders, creams are less stable then emulgel. For example emulsions are thermodynamically unstable because of inappropriate choice of emulsifying agent can occur into phase inversion and sometimes inappropriate formation or arrangement may also result in cracking. So that's why emulgel is approached For avoiding this problem because they are more stable than other topical and transdermal preparations. [32,52,66]
4. **low preparation cost and Production practibility:** production of emulgel is faster growing in both pharmaceutical and cosmetic semisolid topical dosage form because formation of emulgel include of simple and easy steps. In further cases there is no need of expensive materials or instruments, which result in lower production cost. [33,34,45]
5. **Dual control release system:** emulgel shows the reliable path for hydrophobic drugs (o/w emulgel) as well as for hydrophobic drugs (o/w emulgel) [36]. It have dual properties of drug control release of both emulsion & gel.
6. **No need of intensive sonication:** emulgel don't have vesicular molecules because of this emulgel don't needed sonication. Other novel approaches like niosomes and liposome have nano size (vesicular structure) [37, 38]. For defeating the disadvantages of vesicular or nano structure such as lack of efficiency and result in drug degradation and leakage of effects they required intensive sonication.

Emulgel' disadvantages : Emulgel have following disadvantages: [39,40, 61]
1. some drugs cannot permeable or poorly permeable through skin.
2. During the formation of emulgel, it can consist bubbles .
3. incompatibility with large particle size drug.
4. Skin irritation or allergic reaction (inflammation) on contact dermatitis.
5. Applying for long time duration it can causes difficulties during the daily routine work.

II. Materail and Method

Preformulation: Preformulation of Etoricoxib carried out for organoleptic properties, solubility, melting point studies, partition coefficient and spectroscopic determination[12]. Etoricoxib and other additive that used for the development of emulgel for topical application are carried out for their compatibility studies and determined by using infrared spectroscopy. [16, 34, 40]

Solubility is determination of Etoricoxib conduct by the taking 10mg amount of drug into volumetric flask and after that solvent was added to drug into volumetric flask [45]. After that flask was shaked well till the drug was completely solubilise into solvent at room temperature. This process was repetitively carried out with different solvent and then average of every repetitive process was calculate. And finally determine by UV/Visible spectrophotometer. [46, 49]

Melting point of Etoricoxib was determined by Theil's tube melting point apparatus [47,52]. For determination of partition coefficient the ratio of different phases such as organic phase and aqeous phases in which concentration of unionised drug are distributed at equilibrium. example n-octanolol/water. Shake flask method is useful for determination of partition coefficient. [53]

Spectrophotometric scan of etoricoxib:

The stock solution (10 µg/ml) of Etoricoxib was prepared and using pH 5.5 phosphate buffer and scanned between 200-400 nm. The scan concluded lemda max 271 nm in pH 5.5 phosphate buffer. [54, 58]

Preparation of Calibration curve in phosphate buffer 5.5: Various samples with different concentration were examined by the UV spectrophotometry and abs [59, 60]. Of all samples were obtained at the λmax of 271 nm. A graph was plotted (conc. Vs abs.) which resulted a straight line concluding that the drug followed Beer's & lambert's law at the concentration range of 0.2- 1.0 µg/ml.

Drug compatibility studies:

FTIR Analysis: The IR spectra, of pure drug alone and in its combinations with the gelling agents used, were obtained and compared. [63, 71]

Table 1 : FORMULATION DESIGN OF ETORI[53]COXIB OLIVE OIL EMULGEL

Formulation code	F1	F2	F3	F4	F5	F6
Etoricoxib	1 gm	1 gm	1 gm	1 gm	1 gm	1 gm
Olive oil	2 ml	2 ml	2 ml	2 ml	2 ml	2ml
Span 20	0.5 ml	0.5 ml	0.5 ml	0.5 ml	0.5 ml	0.5 ml
Tween 20	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml
Propylene glycol	5 ml	5 ml	5 ml	5 ml	5 ml	5 ml
Methyle paraben	30 mg	30 mg	30 mg	30 mg	30 mg	30 mg
Propyle paraben	30 mg	30 mg	30 mg	30 mg	30 mg	30 mg
Carbopol 934	1% conc.	1.5% conc.	2% conc.	-------	-------	--------
Carbopol 940	------	-------	--------	1% conc.	1.5% conc.	2% conc.
Ethanol	5 ml	5 ml	5 ml	5 ml	5 ml	5 ml
Water	q.s	q.s	q.s	q.s	q.s	q.s
Triethanol amine	q.s	q.s	q.s	q.s	q.s	q.s

Emulgel preparation: There are the following steps for the preparation of Emulgel. [65,67]
1- Gelling agent preparation
2- Emulsion preparation
3- Emulgel preparation

1: Gelling agent preparation: The Carbopol gel was prepared by dispersing different concentration of Carbopol 934 (1%,1.5%, 2%) and carbopol 940 (1%,1.5%, 2%) within decontaminate (purify) water and then continuously stirred at a moderate speed and soaked during overnight. The pH was maintained by triethanol to the skin pH 5.5 and finally maintained the weight to 50gm with purified water. [69, 70]

2: Emulsion preparation: Emulsion are the stable and secure dosage form which helps the oil to be dissolve in water based substances and they are included into liquid component for stable or secure the mixture [70]. Emulsion have two phases first one is Oil phase which is prepared by dissolving span 20 in olive oil and after that heated through heating apparatus. And the other phase which is aqueous phase is prepared by dissolving Tween 20 in water and other side mixed together drug with 5ml ethanol and heated through heating [74]. In other hand the process of mixing Methylparaben, propyl paraben in propylene glycol was performed and after that this mixture was dissolve in aqueous phase. And finally oil phase was encouraged to mix into aqueous phase. and final volume of emulsion was makeup with purified water.

3: Emulgel preparation: Finally achieved emulsion and gel was mixed together and homogenized for 45-60 minutes at moderate speed. After the add the requried triethonal amine to neutralise maintained the pH of emulgel [76,77].

EVALUATION STUDIES OF EMULGELS

Physical appearance: Organoleptic properties of every single one emulgel formulations and marketed formulation of emulgel were evaluated.

The physicochemical properties of the gel formulations are shown in the Tableno.8. From the result it i s clearly evident that all emulgel formulation f1-f6 and market emulgel (Nucoxia emulgel from Zydus cadila) have good homogeneity and consistency [23, 53,78].

Table 2 : Physical appearance data:

Formulation code	Colour	Homogeneity	Consistency	Phase separation
F1	White to Off white	Homogenous	Smooth	-
F2	White to Off White	Homogenous	Smooth	-
F3	White to Off White	Homogenous	Smooth	-
F4	White to Off White	Homogenous	Smooth	-
F5	White to Off White	Homogenous	Smooth	-
F6	White to Off White	Homogenous	Smooth	-
Marketed formulation	White to Off White	Off White	Smooth	-

Rheological studies: The viscosity of emulgel formulation (f1-f6) and marketed emulgel (aroxia) formulation was measured by using Brookfield Viscometer. The optimistic formulation f1 to f3 with carbopol 934 showed the viscosity more than f4 to f6 with carbopol 940.

pH evaluation: The pH values of all emulgel formulations (F1 to F6) range from 6.1 to 6.8, and marketed enulgel formulation (Nucoxia emulgel from Zydus cadila) pH is 6.8. all formulation are measured suitable to avoid the risk of irritation after skin application [14, 50, 80].

Spreadibility: Spreadability of F1,f2,f3 emulgel with gelling agent carbopol 934 was found to be 14.2 g.cm/sec, 13.3 g.cm/sec, 13.6 g.cm/sec respectively, while f4,f5,f6 were found to be 11.6, 12.6 and 12.4g.cm/sec respectively, indicating spreadability of f1-f3 emulgel with carbopol 934 was good as compared f4-f6 emulgel with carbopol 940. And marketed emugel (aroxia) spreadibility was found 13.9 g.cm/sec. Which showed that formulation f1 with carbopol934 (1%) had good spreadibility than marketed emulgel. [43, 57, 81]

Table 3: viscosity determination data, pH studies and Spreadability:

S.N0	Formulation code	Viscosity (rpm)	pH	Spreadability g.cm/sec)
1	**F1**	4589	6.1	14.2
2	**F2**	4853	6.3	13.3
3	**F3**	5853	6.7	13.6
4	**F4**	3211	6.1	11.6
5	**F5**	4304	6.5	12.8
6	**F6**	5304	6.8	12.4
7	**Marketed formulation**	5840	6.8	13.9

Extrudibility: Extrudibility of all formulation f1 to f6 showed in table no 1.3 . where found that f1 with carbopol 934 (1.%) and f4 carbopol940 (1%) having low concentration among their respective formulations shows the low requirement of extrusion pressure and the extrudability grows with the increase in viscosity of the formulation. The formulation with carbopol934 requires low extrusion pressure in comparison with that of carbopol940. F1 formulation with carbopol934 (1%) was found to be more comparable with marketed aroxia emulgel than other formulation (f2-f6) and all the results were acceptable in comparison to the marketed aroxia emulgel. [23, 43, 81]

Swelling index: Formulations with carbopol 934(f1-f3) showed maximum swelling index in comparison with carbopol 940 (f3-f4) and were comparable to that of marketed emulgel. Among all the formulation, F3 emulgel with carbopol 934 (2%) showed the highest swelling index. [26, 37]

Drug content determination: Drug content of the all formulations is determined by UV spectrophotometer, all the formulations shows the drug content in between the limit of 96% to 98% and these all formulation showed the better acceptance and comparable with marketed formulation.[10, 32].

Table 4: Extrudibility data, Swelling index and Drug content determination

S.no.	Formulation code	Extrudibility (g/cm^2)	Swelling index	Mean% ±SD
1	F1	15.4±	30%	96.13±3.89
2	F2	18.2±	34%	92.27±2.3
3	F3	18.3±	45%	97.12±3.2
4	F4	18.9±	29%	91.6±3.1
5	F5	19.1±	35%	94.51±2.3
6	F6	19.6±	30%	93.4±1.2
7	Marketed formulation	15.8±	44%	98.1±3.2

***In-vitro* drug release study and kinetic release:** Drug release of formulations with carbopol 934 and carbopol 940 showed the drug release in given table at the respective time period. And marketed formulation aroxia emulgel shows the drug release after 180 minutes (3 hrs) was 94.88. and found to be that all formulation are comparable with marketed formulation. The release pattern with carbopol 934 emulgel (f2) was better than that of carbopol 940 (f5) because emulgel with carbopol 934 showed maximum drug release than emulgel with carbopol 940 [8, 16, 56].

Table 5: Cumulative % drug release profile of formulated emulgel or marketed emulgel

Time (minute)	F1	F2	F3	F4	F5	F6	Marketed formulation
0	0	0	0	0	0	0	0
30	16.41	38.91	10.51	14.11	23.12	14.65	33.95
60	26.31	46.34	31.97	35.67	47.11	23.45	46.12
90	36.27	55.73	44.35	49.11	55.21	33.72	68.46
120	45.31	79.13	58.27	59.31	67.41	45.11	78.21
150	55.67	89.12	63.32	65.31	75.21	49.57	89.81
180	77.29	95.61	65.32	74.45	80.25	59.51	94.88

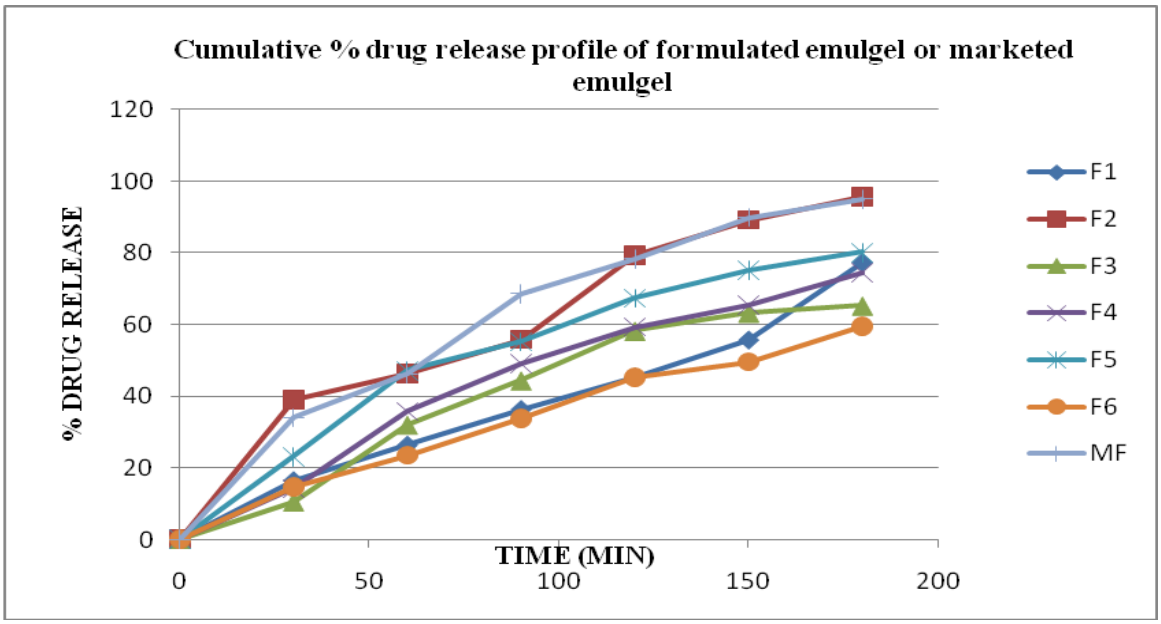

Table 6: Drug kinetic release profile of f2 formulation from Carbopol 934:

Time▼	%CDR▼
0.0	0.00
30.0	38.91
60.0	46.34
90.0	55.73
120.0	79.13
150.0	89.12
180.0	95.61

Model Fitting	R^2	k
Zero order	0.9406	0.5000
1st order	0.9313	-0.0164
Higuchi Matrix	0.9177	9.5730
Peppas	0.9329	2.1169
Hix.Crow.	0.9720	0.0035
Parameters for		
Korsmeyer-Peppas Equation		
n =	0.5402	
k =	2.1169	
Best fit model=	Hixon-Crowell	
Mechanism of release▼		
Anomalous Transport		
where %CDR is % cumulative drug release at time t		

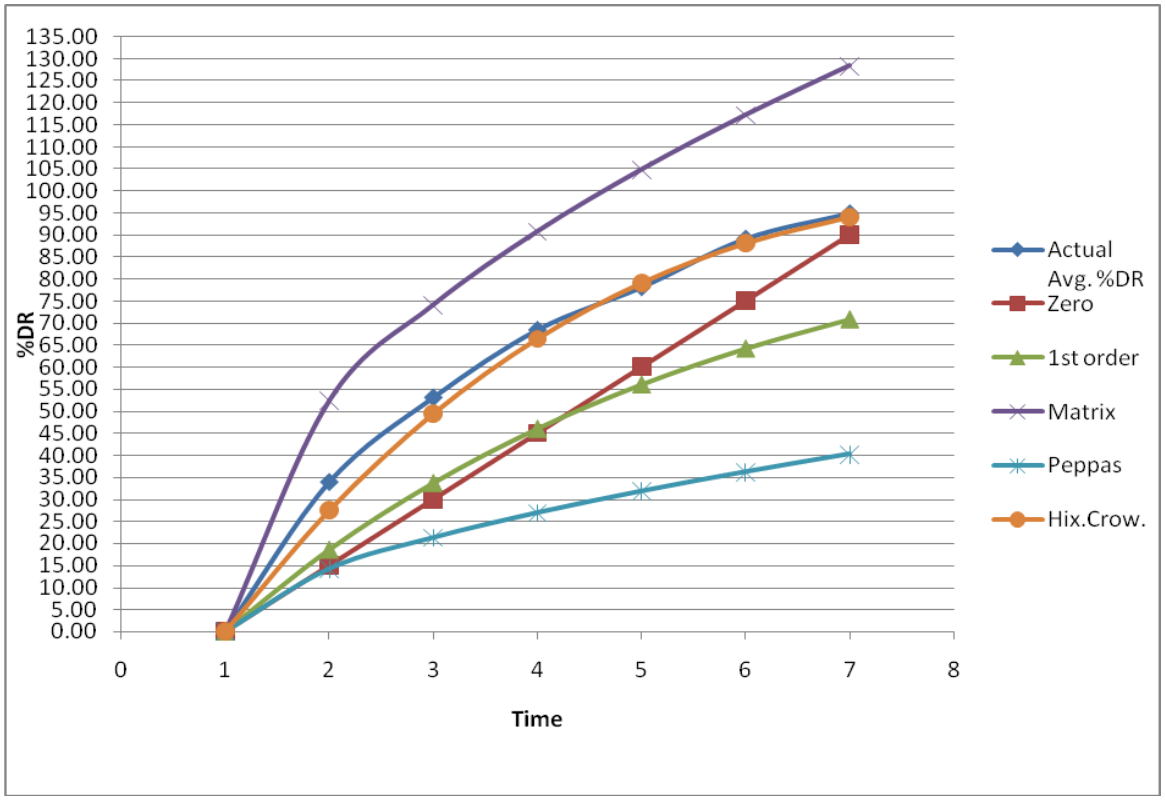

Fig 2: Graph of Cumulative drug release % data of f2 formulation from Carbopol 934:

Table 7: Drug kinetic release profile of marketed formulation (Nucoxia emulgel from Zydus cadila):

Time▼	**%CDR▼**
0.0	0.00
30.0	33.95
60.0	53.12
90.0	68.46
120.0	78.13
150.0	89.12
180.0	94.88

Model Fitting	**R^2**	**k**
Zero order	0.9278	0.5000
1st order	0.9734	-0.0158
Higuchi Matrix	0.9296	9.5707
Peppas	0.9946	1.9877
Hix.Crow.	0.9967	0.0034
Parameters for		
Korsmeyer-Peppas Equation		
n =	0.5793	
k =	1.9877	
Best fit model=	Hixon-Crowell	
Mechanism of release▼		
Anomalous Transport		
where %CDR is % cumulative drug release at time t		

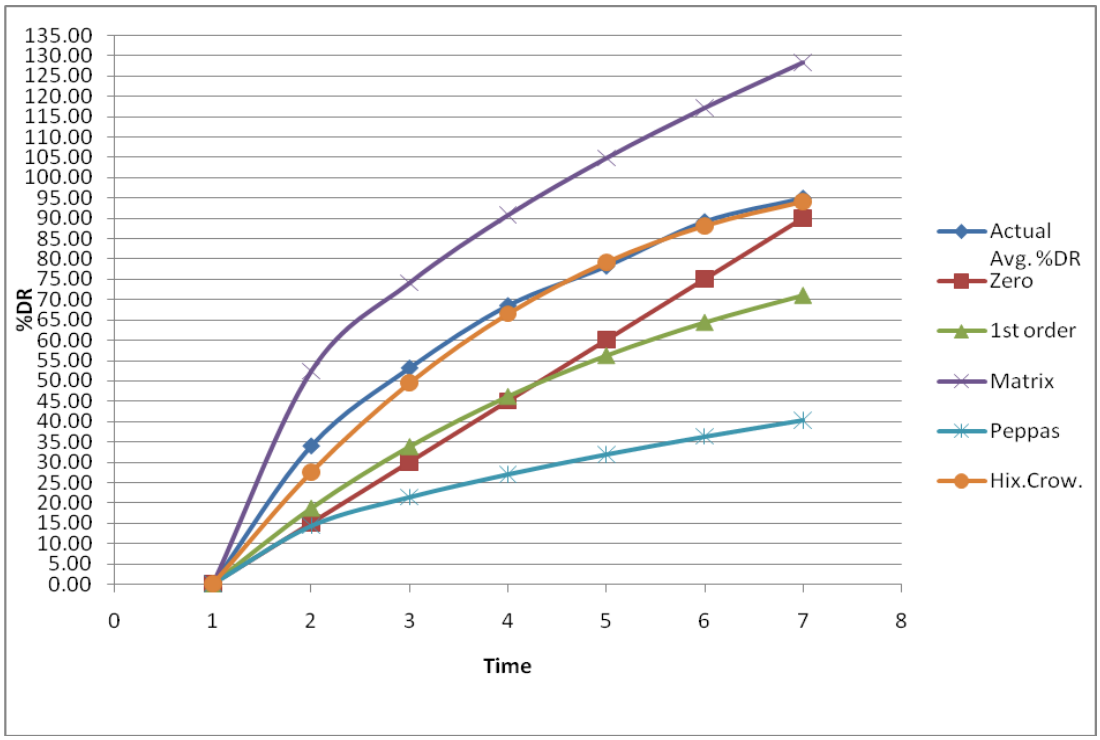

Fig 3: Cumulative % drug release and kinetic release profile of marketed formulation (Nucoxia emulgel from Zydus cadila)

Table 8: Release kinetic result of selected best drug release emulgel formulations and marketed formulation

Formulation	Zero order $\mathbf{R^2}$	1st order $\mathbf{R^2}$	Higuchi Matrix $\mathbf{R^2}$	Peppas $\mathbf{R^2}$	Hix.Crow. $\mathbf{R^2}$	Parameters for korsmeyer-peppas eqn.	Best fit model
F2 (carbopol934)	0.9406	0.9313	0.9177	0.9329	0.9720	n =0.5402 K= 2.1169	Hixon-Crowell
Marketed emulgel formulation	0.9278	0.9734	0.9296	0.9946	0.9967	n =0.5793 K=1.9877	Hixon-Crowell

Accelared Stability studies: Selected formulation f2, f3 carbopol 934 and F5 ,f6 with carbopol 940 and marketed formulation (Nucoxia emulgel from Zydus cadila) was stored for 3 months. After 3 months these formulation were evaluated and they show the acceptable result in their parameters [16].

Table 9: Stability Studies of Formulation at room temp (PBS pH-5.5)

S.N	**Number of day**	**% Drug Remaining**						
		F1	**F2**	**F3**	**F4**	**F5**	**F6**	**Marketed formulation**
1	0	96.55	98.53	95.82	95.96	95.82	95.75	98.76
2	15	96.41	98.37	95.72	95.78	95.67	95.71	98.68
3	30	96.77	98.21	95.63	95.56	95.55	95.66	98.61
4	45	96.37	97.06	95.47	95.43	95.47	95.46	98.54
5	60	95.15	97.11	95.37	95.28	95.21	95.34	98.42
6	75	95.10	97.41	95.13	95.11	94.96	95.29	98.37

III. Conclusion

Etoricoxib emulgel was successfully perform the acceptance and comparable with marketed formulation (Nucoxia emulgel from Zydus cadila). Etoricoxib emulgel formulation had consist the oil phase of olive oil which is successfully incorporated with aq.phase. all formulation of different gelling agents including carbopol 934 and carbopol 940 with different concentration showed the acceptable properties, acceptable evaluation parameters such as pH, spreadibility, swelling index, viscosity, kinetic and drug release and stability studies which have no changed after the storage of 3 months.

F2 formulation from carbopol 934 showed the high drug release content comparatively f5 formulation from carbopol 940 .And finally carbopol 934 showed the drug releae content which is comparable to marketed emulgel (Nucoxia emulgel from Zydus cadila) formulation. In present situation this technique for TDDS getting part of qualities and might be demonstrated the best strategy in future.

Conflict of interest: Nil

IV. Acknowledgment

Author very thankful to guide and faculty of Gyani inder singh institute of professional studies, Dehradun, Uttarakhand. Author also thankful to Mr. Vijay singh bisht for providing the drug sample, from sun pharmaceutical, paonta sahib, Himachal Pradesh, India. Author and coauthor again last but not least thankful to Gyani inder singh institute for providing the all facilities and equipment for carried out the all research work.

References

[1]. Aher SD, Banerjee SK, Gadhave MV, Gaikawad DD. Emulgel: A New Dosage Form for Topical Drug Delivery. International Journal of Institutional Pharmacy and Life Sciences, 2013: 3(3); 1-10.
[2]. Alla AA. Glucosamine sulphate transdermal gels: An alternative route for drug delivery. Int J Pharm Res Dev. 2012: 3(11); 102-113.
[3]. Amrutha B, Kumbhar. In situ gel forming injectable drug delivery system. International journal of pharmaceutical sciences and research. 2013: 4(2); 597-609.
[4]. Arpan AS, Kamal K, Rushabh S and Rajesh A, Keraliya. Emulgel: A Topical Preparation for Hydrophobic Drugs. Pharma Tech Medica. 2013: 2(5); 370- 376.
[5]. Ana ML, Elizangela A, Andre LMC, Ruth RS, Miracy MA, Almir GW. Development of lapachol topical formulation: anti-inflammatory study of a selected formulation. AAPS Pharm Sci Tech. 2008: 9(1); 163-168.
[6]. Ankur J, Piyusha De, Naveen V, Jitendra C, Hemant K, Sanjay J. Development of antifungal emulsion based gel for topical fungal infections. Int J Pharm Res Dev. 2011: 2 (12); 18-25.
[7]. Langdon BA, Mullarney MP, Menthol. Handbook of Pharmaceutical excipients. 5th ed., 2005; 459461.
[8]. Banker GBS, Rodes CT. Modern Pharmacist. Marcel Dekker, New York, 1979: 40(2); 263-311.
[9]. Bhatt P, Gnanaranjan G. Emulgel- A Novel Formulation Approach for Topical Delivery of Hydrophobic Drugs. International Research Journal of Pharmacy. 2013: 4(2); 12-16.
[10]. Cecv G. Preclinical characterization of NSAIDs on ultra-deformable carriers or conventional topical gels. International Journal of Pharmaceutics. 2008; 20-35.
[11]. Clive P, Michael J, Curtis, Morley S, Michael W. Brian Hoffman. Farmacología integrada (in Spanish). Published by Elsevier España. 1998. ISBN 84-8174-340-2.
[12]. Doaa E, Sahar ME. Ketorolac trometamol topical formulation: release behavior physical characterization skin permeation efficacy and gastric safety. J.Pharm Pharmacol. 2010: 62; 25-34.

[13]. Jerry MZ. Macrolides and Ketolides: Azithromycin, Clarithromycin, Telithromycin. Infect Dis Clin N Am 2004; 18: 621-649.
[14]. Sood KS. Macrolides: Clarithromycin and Azithromycin. Seminars in pediatric infectious disease, vol 10(1) January, 1999: pp.23-30.
[15]. Sams WW JR, Lynch PJ. Principles and practice of dermatology. 2nd ed. New York, Churchill Livingstone, 1990.
[16]. Leung AK, Robosn WL. Acne J Soc Health 1991; 111: 57-60.
[17]. Bashir A, Mujahid TY, Jehan N. Antibiotic resistance profile: Isolation and characterization of clinical isolates of staphylococci from patients with community- Acquired skin infections. Pak J Pharm Sci 2007; 20(4): 295-299.
[18]. Mohamed MI. Topical emulsion gel composition comprising diclofenac sodium. Am Assn Pharm Sci 2004; 6(3) :1-7.
[19]. Joel LZ, Gregory PK. In: Liberman HA, Rieger MM, Banker GS (eds): Pharmaceutical dosage forms: disperse systems, Marcel Dekker, New York, 1989, 2, 502.
[20]. Amnon C, Shafir B. Transdermal drug delivery using microemulsion and aqueous systems: Influence of skin storage condition on the in vitro permeability of Diclofenac from aqueous vehicle systems. Int J Pharmaceut 2006; 311(1-2): 55-62.
[21]. Patel GC, Patel MM. Preliminary evaluation of Sesbania seed gum mucilage as gelling agent. Int J Pharm Tech Res 2009; 1(3): 840-843.
[22]. Kesavan B, Jayaraman A. Lipid nanoparticles for transdermal delivery of flurbiprofen: Formulation in-vitro, ex-vivo and in-vivo studies. Lipids health Dis 2009; 8: 6.
[23]. Ambala R, Vemula SK. Formulation and characterization of ketoprofen emulgels. J Appl Pharm Sci 2015;5:112-7.
[24]. Pednekar A, Dandagi P, Gadad A, Mastiholimath V. Formulation and characterisation of meloxicam loaded emulgel for topical application. Int J Pharm Pharm Sci 2015;7:216-22.
[25]. Ajazuddin, Alexander A, Khichariya A, Gupta S, Patel RJ, Giri TK, et al. Recent expansions in an emergent novel drug delivery technology: emulgel. J Controlled Release 2013;171:122-32.
[26]. Tripathi KD. Essentials of medical pharmacology. 6th ed. New Delhi: Jaypee publishers; 2008.
[27]. Clissold SP, Heel RC. Tioconazole a review of its antimicrobial activity and therapeutic use in superficial mycoses. Drugs 1986;31:29-51.
[28]. Rathnanand M, Khatri SK, Nikhila R. Formulation and evaluation of wound healing activity of linezolid topical preparations on diabetic rats. Int J Appl Pharm 2016;8:30-6.
[29]. Mohamed MI. Optimization of chlorphenesin emulgel formulation. AAPS J 2004;6:1-7.
[30]. Kumar V, Antil M, Singh J, Kumar D. Emulgel-novel topical drug delivery system–a comprehensive review. Int J Pharm Sci Res 2016;7:4733-42.
[31]. Khan WA, Kotta S, Ansari SA, Sharma RK, Kumar A, Ali J. Formulation development, optimization and evaluation of aloe vera gel for wound healing. Pharmacogn Mag 2013;9:6-10.
[32]. Khambete H, Deveda P, Jain A, Vyas N, Jai S. Gellified emulsion for sustain delivery of itraconazole for topical fungal diseases. Int J Pharm Pharm Sci 2010;2:104-12.
[33]. Ashara KC, Paun JS, Soniwala MM, Chavada JR, Mori NM. Microemulsion based emulgel: a novel topical drug delivery system. Asian Pac J Trop Dis 2014;4:27-32.
[34]. Kundan PJ, Laxman DS, Eknath PK. Stability evaluation of topical ointment comprising calcipotriol and prednicarbate. Int Res J Pharm 2015;6:43-7.
[35]. Sundari PP, Mullapudi D, Srinivas P. Formulation and evaluation of anti-arthritic poly herbal emulgel. Int J Pharm Technol 2014;6:6608-21.
[36]. Kumar P, Bisht T, Samanta J . Formulation evaluation and optimization of niosomal gel of piroxicam. IOSR journal of pharmacy 2019; 9(5): 1-7.
[37]. Saxena A, Singh R. A review on levofloxacin in situ-gel formulation. Asian J Pharm Clin Res 2015;8:37-41.
[38]. Ali-Shtayeh MS, Abu Ghdeib SI. Antifungal activity of plant extracts against dermatophytes. Mycoses 1999;42:665–72.
[39]. Designing and evaluation of dual release bi-layer of aceclofenac optimized by SSG and combination of HPMC K4M and PVP k30. IOSR journal of pharmacy 2016; 11 (5): 7-15.
[40]. Mulye SP, Wadkar KA, Kondawar MS. Formulation development and evaluation of Indomethacin emulgel. Pharm Sinica 2013;4:31-45.
[41]. Ghodekar SV, Chaudhari SP, Ratnaparakhi MP. Development and characterization of silver sulfadiazine emulgel for topical drug delivery. Int J Pharm Pharm Sci 2012;4:305-16.
[42]. Sood KS. Macrolides: Clarithromycin and Azithromycin. Seminars in pediatric infectious disease, vol 10(1) January, 1999: pp.23-30.
[43]. Sams WW JR, Lynch PJ. Principles and practice of dermatology. 2nd ed. New York, Churchill Livingstone, 1990.
[44]. Leung AK, Robosn WL. Acne J Soc Health 1991; 111: 57-60.
[45]. Bashir A, Mujahid TY, Jehan N. Antibiotic resistance profile: Isolation and characterization of clinical isolates of staphylococci from patients with community- Acquired skin infections. Pak J Pharm Sci 2007; 20(4): 295-299.
[46]. Mohamed MI. Topical emulsion gel composition comprising diclofenac sodium. Am Assn Pharm Sci 2004; 6(3) :1-7.
[47]. Principle of skin therapy. Website: http// www.dermweb.com/therapy /common.htm. Accessed on 28 May 2011.
[48]. Joel LZ, Gregory PK. In: Liberman HA, Rieger M, Banker GS (eds): Pharmaceutical dosage forms: disperse systems, Marcel Dekker, New York, 1989, 2, 502.
[49]. Amnon C, Shafir B. Transdermal drug delivery using microemulsion and aqueous systems: Influence of skin storage condition on the in vitro permeability of Diclofenac from aqueous vehicle systems. Int J Pharmaceut 2006; 311(1-2): 55-62.
[50]. Patel GC, Patel MM. Preliminary evaluation of Sesbania seed gum mucilage as gelling agent. Int J Pharm Tech Res 2009; 1(3): 840-843.
[51]. Kesavan B, Jayaraman A. Lipid nanoparticles for transdermal delivery of flurbiprofen: Formulation in-vitro, ex-vivo and in-vivo studies. Lipids health Dis 2009; 8: 6.
[52]. Tominaga Naito SH. Percutaneous absorption ofDiclofenac sodium ointment. Int J Pharm 1985; 24: 115-124.
[53]. Baibhav J, Singh G, Rana A C, Saini S, Singla V: Emulgel: A comprehensive review on recent advancement on topical drug delivery. IRJP, 2011; 2(11): 66-70.
[54]. Aher S. D, Banerjee S.K, Gadhave M.V, Gaikawad D.D: Emulgel: a new dosage form for topical drug delivery.IJIPLS. 2013; 3(3): 1-10.
[55]. Prajapati Mehulkumar N, Patel M R, Patel K R and Patel N M: Emulgels: a novel approach to topical drug delivery. IJUPBS. 2013; 2(1): 134-148.
[56]. Panwar AS, Upadhyay N, Bairagi M, Gujar S, Darwhekar GN, Jain DK. Emulgel: A review. Asian J Pharm Life Sci. 2011; 1(3): 333-343.

[57]. Garg A, Aggarwal D, Garg S, and Singla AK (2002). Spreading of Semisolid Formulations: An Update. *Pharmaceutical Technology*. Circle/eINFO
[58]. Available at:http://www.pharmtech.com/pharmtech/data/articlestandard//pharmtech/362002/ 30365/article.pdf
[59]. Khalil YI, Khasraghi AH, Mohammed EJ. Preparation and evaluation of physical and, rheological properties of clotrimazole emulgel: Iraqi J Pharm Sci. 2011; 20(2): 19-27.
[60]. Baibhav J, Singh G, Rana A. C, Saini Seema, Singla Vikas,: Emulgel: A Comprehensive Review on The Recent Advances In Topical Drug Delivery, International Research Journal of Pharmacy. (2011; 2(11): 66-70.
[61]. Trommer H, Neubert RHH: Overcoming the stratum corneum the modulation of skin penetration. Skin Pharmacol Physiol.2006; 19:106-121.
[62]. Singla V, Saini S, Joshi B, Rana A.C, : Emulgel: A New Platform for Topical Drug Delivery International Journal of Pharma and Bio Sciences, 3(1); 21-29.
[63]. Washitake M, Takashima Y, Tanaka S, Anmo T, Tanaka I Drug permeation through egg shell membranes. Chern. Pharm. *Bull.1980;* 28:2855-2861.
[64]. ICH Harmonized Tripartite Guidelines, Stability Testing of New Drug Substances and Products. ICH Committee 2003; 8.
[65]. Singh J, Gupta S, Kaur H. Prediction of in vitro drug release mechanisms from extended release matrix tablets using SSR/R2 technique. Trends in applied science research 2011;6(4) :400-409.
[66]. Pinheiro IM, Carvalho IP, de Carvalho CES, Brito LM, da Silva ABS, Conde Júnior AM, et al. Evaluation of the in vivo leishmanicidal activity of amphotericin B emulgel: An alternative for the treatment of skin leishmaniasis. Exp Parasitol 2016; 164; 49-55.
[67]. Singh VK, Yadav I, Kulanthaivel S, Roy B, Giri S, Maiti TK, et al. Groundnut oil based emulsion gels for passive and iontophoretic delivery of therapeutics. Des Monomers Polym 2016:1-12.
[68]. Zhang H, Cui B, Qian X, Fan H, Feng X. Preparation of amlodipine besylate emulgels for transdermal administration and its percutaneous permeability in vitro. Chin J New Drugs 2016; 25(3).
[69]. Jacobs GA, Gerber M, Malan MM, Du Preez JL, Fox LT, Du Plessis J. Topical delivery of acyclovir and ketoconazole. Drug Deliv 2016; 23(2):641-651.
[70]. Soliman SM, Abdelmalak NS, El-Gazayerly ON, Abdelaziz N. Novel non-ionic surfactant proniosomes for transdermal delivery of lacidipine: optimization using 23 factorial design and in vivo evaluation in rabbits. Drug Deliv 2016:1-15.
[71]. Burger C, Gerber M, Du Preez JL, Du Plessis J. Optimised transdermal delivery of pravastatin. Int J Pharm 2015; 496(2):518-525.
[72]. Mallick SP, Sagiri SS, Singh VK, Behera B, Thirugnanam A, Pradhan DK, et al. Genipin-Crosslinked Gelatin-Based Emulgels: an Insight into the Thermal, Mechanical, and Electrical Studies. AAPS PharmSciTech 2015; 16(6):1254-1262.
[73]. Nivsarkar M, Maroo SH, Patel KR, Patel DD. Evaluation of skin penetration of diclofenac from a novel topical non aqueous solution: A comparative bioavailability study. J Clin Diagn Res 2015; 9(12):FC11-FC13.
[74]. Hamed R, Basil M, AlBaraghthi T, Sunoqrot S, Tarawneh O. Nanoemulsion-based gel formulation of diclofenac diethylamine: design, optimization, rheological behavior and in vitro diffusion studies. Pharm Dev Technol 2015.
[75]. Daudt RM, Back PI, Cardozo NSM, Marczak LDF, Külkamp-Guerreiro IC. Pinhão starch and coat extract as new natural cosmetic ingredients: Topical formulation stability and sensory analysis. Carbohydr Polym 2015; 134:573-580.
[76]. Dong L, Liu C, Cun D, Fang L. The effect of rheological behavior and microstructure of the emulgels on the release and permeation profiles of Terpinen-4-ol. Eur J Pharm Sci 2015; 78:140-150.
[77]. Kong X, Zhao Y, Quan P, Fang L. Development of a topical ointment of betamethasone dipropionate loaded nanostructured lipid carrier. Asian J Pharm Sci 2015.
[78]. Digennaro R, Pecorella G, La Manna S, Alderisio A, Alderisio A, De Pascalis B, et al. Prospective multicenter observational trial on the safety and efficacy of LEVORAG® Emulgel in the treatment of acute and chronic anal fissure. Tech Coloproctol 2015;19(5):287-292.
[79]. Shen Y, Ling X, Jiang W, Du S, Lu Y, Tu J. Formulation and evaluation of Cyclosporin A emulgel for ocular delivery. Drug Deliv 2015;22(7):911-917.
[80]. Pednekar A, Dandagi P, Gadad A, Mastiholimath V. Formulation and characterisation of Meloxicam loaded emulgel for topical application. Int J Pharmcy Pharm Sci 2015;7(11):216-222.
[81]. Singh C, Sharma P, Bal T, Ghosh M, Dubey R, Das S. Preparation and evaluation of Radiosensitizing agent Nimorazole in topical emulgel. Der Pharm Lett 2015;7(9):132-142.
[82]. Nikumbh KV, Sevankar SG, Patil MP. Formulation development, in vitro and in vivo evaluation of microemulsion-based gel loaded with ketoprofen. Drug Deliv 2015;22(4):509-515.
[83]. Naga Sravan Kumar Varma V, Maheshwari PV, Navya M, Reddy SC, Shivakumar HG, Gowda DV. Calcipotriol delivery into the skin as emulgel for effective permeation. Saudi Pharm J 2014;22(6):591-599.
[84]. Phutane KR, Patil SS, Adnaik RS, Nitalikar MM, Mohite SK, Magdum CS. Design and development of allopurinol emulgel. Res J Pharm Technol 2014;7(7):733-736.

IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS) is UGC approved Journal with Sl. No. 5012, Journal no. 49063.

Ankita Negi " Formulation and Characterization of Etoricoxib Olive Oil Emulgel by Using Different Gelling Agents" IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS) 14.6 (2019): 26-36.