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Research

Formulation Development And Invitro Evaluation Of Etoricoxib Emul Gels

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Abstract

Topical drug delivery system (TDDS) facilitates the passage of therapeutic quantities of drug substance through the skin and into the general circulation for their systemic effects. Evidence of percutaneous drug absorption may be found through measurable blood levels of the drug, detectable excretion of the drugs and its metabolites in the urine and clinical response of the patient to the therapy. The purpose of topical dosage form is to conveniently deliver drug across a localized area of the skin. To develop an ideal dosage form, one must take into account flux of the drug across the skin, nature of drugs, patient acceptability of the formulation etc.

Although having plenty of advantages over other routes of administration topical drug delivery system is having certain limitations including hydrophilic drugs cannot easily penetrate across skin, to overcome this problem drug made into sufficient lipophilic or lipophilic drugs are used along with certain penetration enhancers which help to achieve desired results. On this contest, emulgel was formulated using carbopol 934 and HPMC K15M, clove oil / Castrol oil as oil phase, emulsifying agents like tween 20 and span 20and propylene glycol as permeation enhancers.

Keywords: Emul gels, Sonication, HPMC K 15, TWEEN 20, SPAN 20.

INTRODUCTION

Optimization of drug delivery through human skin is important in modern therapy. Recently, the transdermal route vied with oral treatment as the most successful innovative research area in drug delivery[1].

Transdermal delivery is an important delivery route that delivers precise amount of drug through the skin for systemic action. Improved methods of drug delivery for biopharmaceuticals are important for two reasons; these drugs represent rapidly growing portion of new therapeutics, and are most often given by injection[2,3]. Discovery of new medicinal agents and related innovation in drug delivery system have not been only enabled the successful implementation of novel pharmaceutical, but also permitted the development of new medical treatment with existing drugs[4]. Throughout the past two decades, the transdermal patcheshas become a proven technology holding the promise

that new compound could be delivered in a safe and convenient way through the skin. Since the first transdermal patch was approved in 1981 to prevent nausea and vomiting associated with motion sickness, the FDA has approved through the past 22 years more than 35 transdermal patch products spanning 13 molecules[5].

Routes of penetration

At the skin, molecules contact cellular debris, microorganisms, sebum and other materials, which negligibly affect permeation. The penentration has three potential pathways to the viable tissue - through hair follicles with associated sebaceous glands, via sweat ducts, or across continuous stratum corneum between these appendages[6].

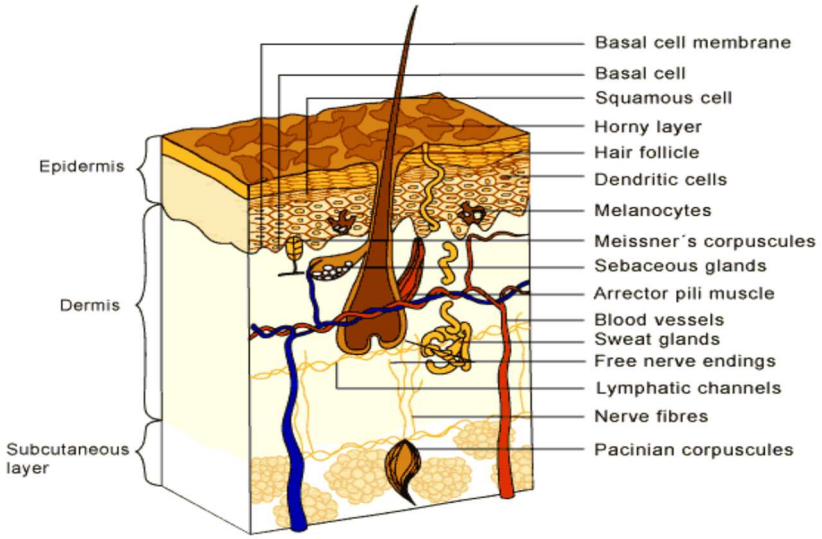


Fig 1: Structure of skin

Ethosomes

The vesicles have been well known for their importance in cellular communication and particle transportation for many years. Researchers have been understanding the properties of vesicle structures for use in better drug delivery within their cavities, that would allow to tag the vesicle for cell specificity. Vesicles would also allow to control the release rate of drug over an extended time, keeping the drug shielded from immune response or other removal systems and would be able to release just the right amount of drug and keep that concentration constant for longer periods of time. One of the major advances in vesicle research was the finding a vesicle derivative, known as an ethosomes[7,8].

Ethosomal carriers are systems containing soft vesicles and are composed mainly of phospholipid (Phosphotidyl choline; PC), ethanol at relatively high concentration and water. It was found that ethosomes penetrate the skin and allow enhanced delivery of various compound to the deep strata of the skin or to the systemic circulation.[9,10]

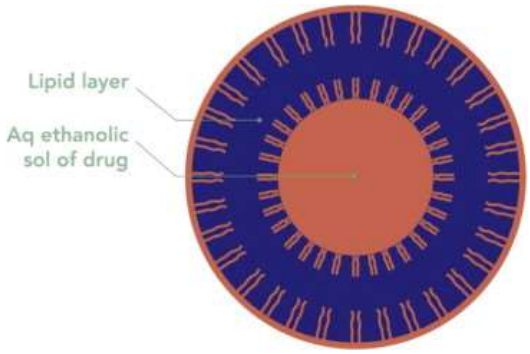
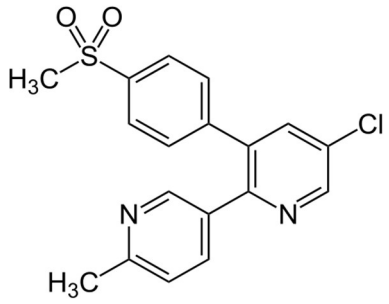


Fig 2: Structure of ethosomes

Drug profile

Etoricoxib (**Arcoxia**) is a selective COX-2 inhibitor from Merck & Co. Currently it is approved in more than 80 countries worldwide but not in the US, where the Food and Drug Administration (FDA) has required additional safety and efficacy data for etoricoxib before it will issue approval.



Structure:Etoricoxib Drug
Chemical Formula: $C_{18}H_{15}ClN_2O_2S$
Weight: Average: 358.842

Synonyms

- Etoricoxib
- étoricoxib
- Etoricoxibum

Half-life: 22 hours

METHODOLOGY

Table 1: List of chemicals used

Chemicals	Source
Etoricoxib API	Provided by Chandra labs, Hyderabad
Carbopol 934	Research lab fine chem, Mumbai
Light liquid paraffin	Research lab fine chem, Mumbai
Tween 20	Research lab fine chem, Mumbai
Span 20	Research lab fine chem, Mumbai
Propylene glycol	Research lab fine chem, Mumbai
Ethanol	Research lab fine chem, Mumbai
Methyl paraben	Research lab fine chem, Mumbai
Propyl paraben	Research lab fine chem, Mumbai
Clove oil	Sigma Oils, Hyderabad
Castrol Oil	Sigma Oils, Hyderabad

Table 2: List of instruments used

Digital electronic balance	Essae, Bangalore
Magnetic stirrer	REMI, Mumbai
UV-Visible spectrophotometer	Shimadzu 1800, Japan
FTIR spectrophotometer	Shimadzu 8400, Japan
Digital pH meter	EI, Hariyana
Melting point apparatus	EI, Hariyana
Brookfield viscometer	Brookfield SynchroLectric Viscometer
Spreadability apparatus	Local manufacturers
Scanning electron microscopy	Shimadzu SSX-550, Japan

Analytical method development
Identification and authenticity of Etoricoxib pure drug
Physical appearance
Physical appearance of the drug was examined by organoleptic properties, such as color, taste, odor and state.

Determination of melting point
Melting point of the drug was determined by taking small quantity of drug in a capillary tube closed at one end which was then place in Tehsil's melting point apparatus. The temperature at which the drug melts was noted using liquid paraffin as liquid solvent. Average of triplicate readings was recorded.

Infrared spectral studies
Infrared spectroscopy deals with the infrared region of the electromagnetic spectrum. FTIR is most useful tool for identifying chemicals that are either organic or inorganic by identifying the types of chemical bonds (functional groups).In this technique 2-3mg of drug was allowed to mixed with about 0.5-1gm of KBr (transparent to IR) and then thoroughly grind the mixture in a motor, press the mixture in a pellet die manually and place it in Fourier Transform Infrared (FTIR) spectrophotometer (Shimadzu corporation 8400S, Japan).

RESULTS

Identification of authenticity of Etoricoxib pure drug
Physical appearance
Physical appearance of the drug was examined by organoleptic properties and results were obtained as follows:

- **Color:** White or almost white
- **Odor:** Odorless
- **Taste:** Bitter
- **State:** Fine powder

Determination of melting point

Table 3: Melting point

Compound name	Melting point (^{0}C)	
	Standard	Observed
Etoricoxib	134-135 °C 134^{0}C -138^{0}C	135^{0}C

Standard calibration curve

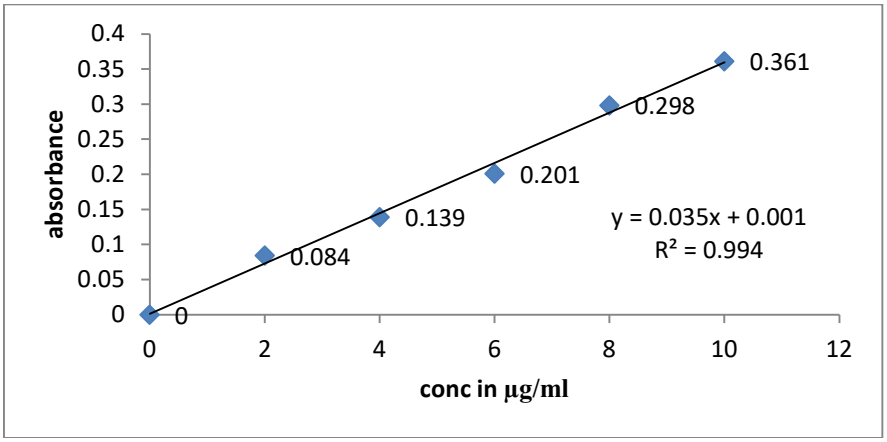


Fig 3: Standard Graph ofEtoricoxib in Phosphate Buffer pH 7.4

Pre-formulation studies
FTIR spectroscopy

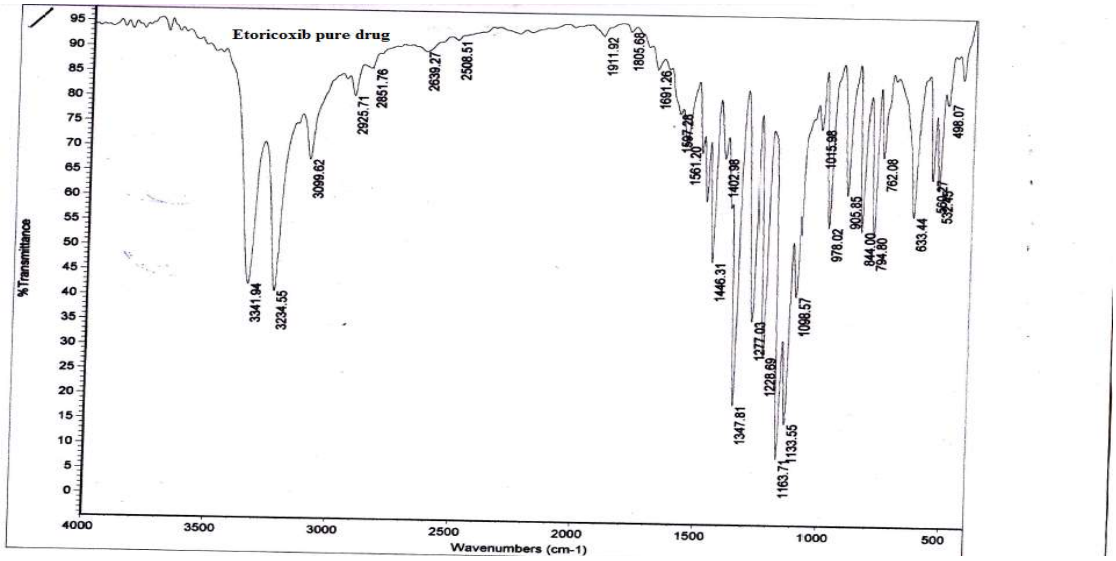


Fig4: FTIR of Etoricoxib pure drug

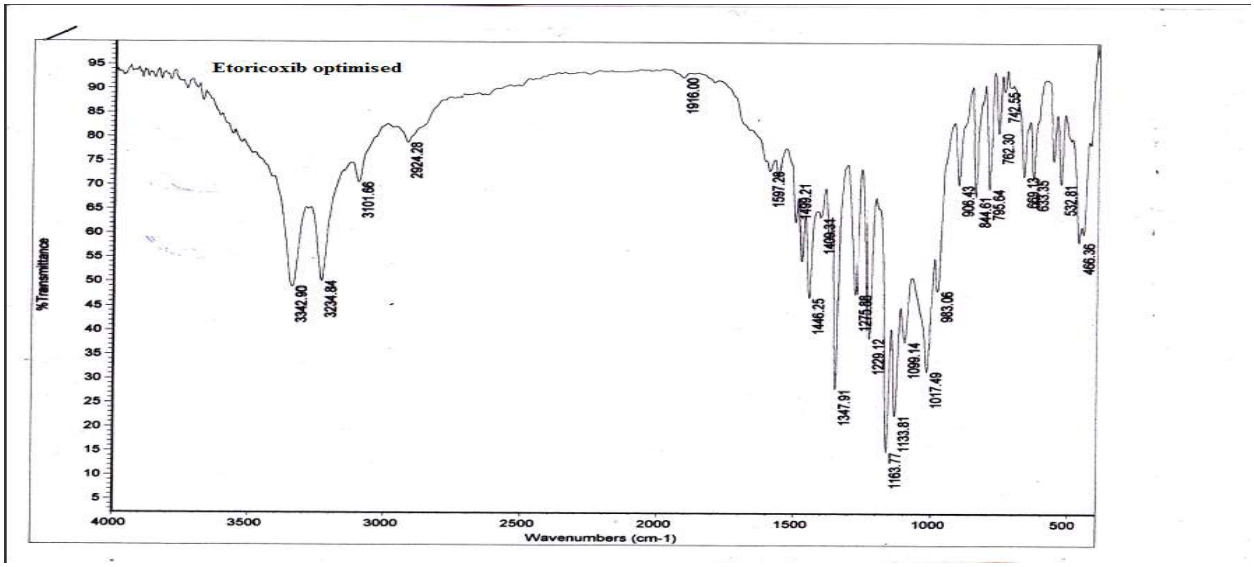


Fig 5: FTIR of Etoricoxib optimized formulation F7

Evaluation parameters
Physical appearance

Table 4: Physical appearance data

Formulation code	Color	Homogeneity	Consistency	Phase separation
F1	Creamy white	Homogenous	Smooth	-
F2	Creamy white	Homogenous	Smooth	-
F3	Creamy white	Homogenous	Smooth	-
F4	Creamy white	Homogenous	Smooth	-
F5	Creamy white	Homogenous	Smooth	-
F6	Creamy white	Homogenous	Smooth	-

F7	Creamy white	Homogenous	Smooth	-
F8	Creamy white	Homogenous	Smooth	-

pH determination

Table 5: pH determination data

Sl.no	Formulation code	pH
1	F1	5.31
2	F2	5.22
3	F3	5.47
4	F4	5.50
5	F5	5.48
6	F6	5.32
7	F7	5.61
8	F8	5.56

Spreadability studies

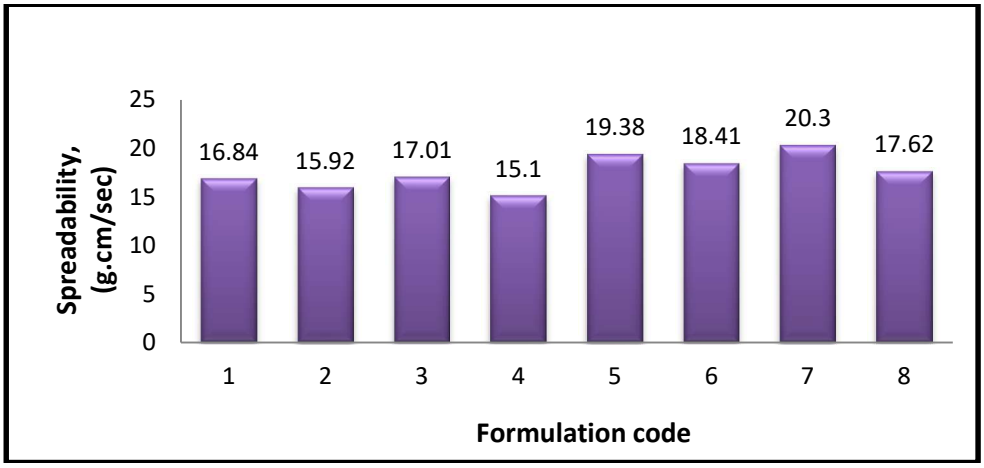


Fig 6: Graph for spreadability (F1 to F8)

Rheological studies (10rpm)

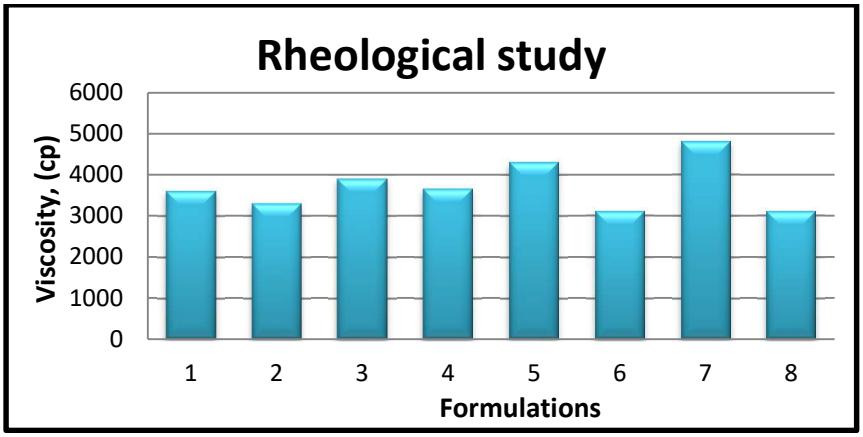


Fig 7: Rheogram for formulations F1 to F8

Extrudability studies

Table 6: Data for extrudability for F1 to F8

Sl.no	Formulation code	Extrudability
1	F1	Easily extrudable
2	F2	Easily extrudable
3	F3	Easily extrudable
4	F4	Easily extrudable
5	F5	Easily extrudable
6	F6	Easily extrudable
7	F7	Easily extrudable
8	F8	Easily extrudable

Drug content determination

Table 7: Drug content data for F1 to F8

Sl.no	Formulation code	Mean% ± SD
1	F1	91.74±3.9
2	F2	90.27±2.3
3	F3	91.50±3.2
4	F4	90.50±1.9
5	F5	90.43±2.1
6	F6	92.51±1.9
7	F7	93.12±2.3
8	F8	89.6±3.1

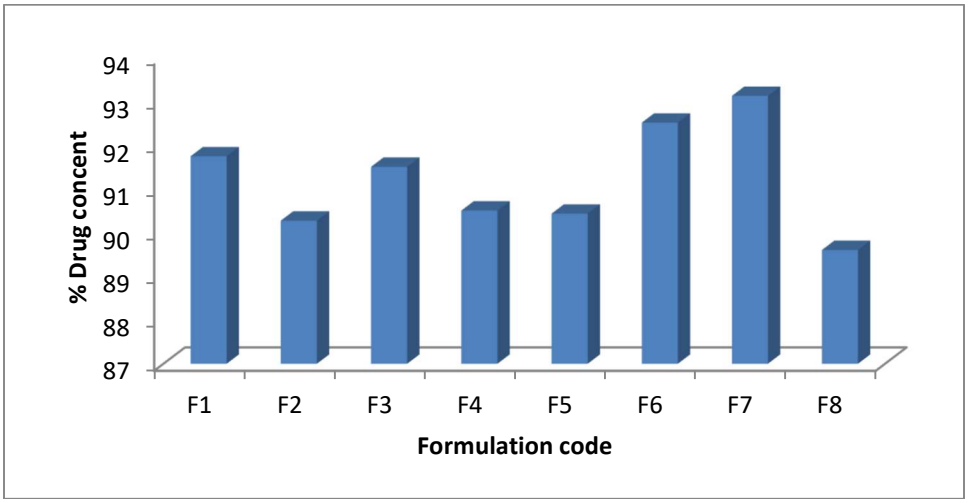


Fig 8: Graph for drug content (F1 to F8)

In-Vitro Drug permeation data

Table 8: % cumulative drug release data for F1 to F8

Time (hrs)	% Cumulative drug release							
	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	**0**	0
1	6.17	5.56	4.10	5.18	7.01	3.94	**7.80**	4.76
2	10.82	8.61	7.25	7.93	13.42	6.15	**16.51**	7.51
3	17.54	13.25	10.93	12.45	25.08	9.37	**29.72**	11.05

4	25.26	19.13	12.28	17.62	32.75	11.20	**38.64**	16.54
5	32.47	26.58	23.68	26.01	38.62	22.46	**47.38**	25.93
6	40.31	34.40	28.41	32.85	45.27	25.34	**55.13**	30.24
7	49.07	42.79	33.06	42.56	56.91	29.81	**63.02**	38.85
8	58.46	49.83	37.12	46.42	62.84	34.65	**70.61**	40.69
9	62.02	52.32	42.62	49.83	68.56	40.65	**77.54**	45.65
10	68.32	59.82	49.53	52.64	76.85	46.74	**82.25**	52.25
11	73.65	63.25	53.62	57.45	80.25	51.05	**86.45**	55.48
12	75.86	69.53	59.31	61.26	84.32	57.29	**88.47**	60.12

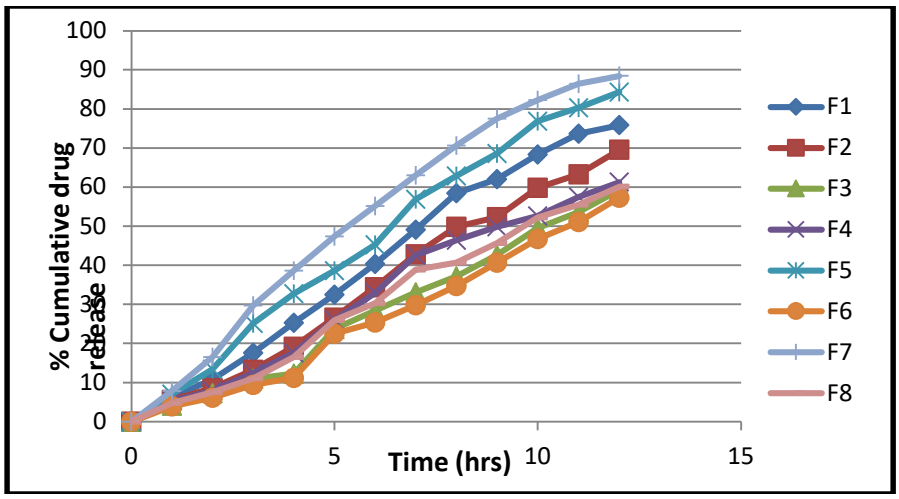


Fig 9: In vitro drug permeation graph (F1 to F8)

SUMMARY AND CONCLUSION

Topical drug delivery system (TDDS) facilitates the passage of therapeutic quantities of drug substance through the skin and into the general circulation for their systemic effects. Evidence of percutaneous drug absorption may be found through measurable blood levels of the drug, detectable excretion of the drugs and its metabolites in the urine and clinical response of the patient to the therapy.

Although having plenty of advantages over other routes of administration topical drug delivery system is having certain limitations including hydrophilic drugs cannot easily penetrate across skin, to overcome this problem drug made into sufficient lipophilic or lipophilic drugs are used along with certain penetration enhancers which help to achieve desired results. On this contest, emulgel was formulated using carbopol 934 and HPMC K15M, clove oil / Castrol oil as oil phase, emulsifying agents like tween 20 and span 20 and propylene glycol as permeation enhancers.

On basis of quality of emulgel produces total eight formulations F1 to F8 were selected. They were evaluated for physical appearance, pH, rheological study, spreadability, drug content and in-vitro drug permeation study.Thus, the formulated emulgel had a distinct advantage over existing conventional dosage form in that the drug permeation was found to be rapid across the skin and hence the increased therapeutic response by bypassing 1st pass metabolism and with no gastro intestinal bleeding and also patient compliance.

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