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Research Article

Formulation And Evaluation of Orphenadrine Nanogel

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ABSTRACT

Nanogels have emerged as advanced drug delivery systems owing to their high water content, biocompatibility, and ability to provide controlled release. The present study was designed to investigate the potential of nanogel formulations for enhancing the topical delivery of Orphenadrine, a centrally acting muscle relaxant. Nanoparticles were first prepared using the solvent evaporation method, where Eudragit S100 served as the polymer, and surfactants (SPAN 80 and TWEEN 80) were employed to stabilize the formulations. Carbopol 940 and HPMC were incorporated as gelling agents to form nanogels at different concentrations. The effect of surfactant type on nanoparticle characteristics and the influence of polymeric gel bases on drug release were systematically evaluated. The prepared formulations were characterized for particle size, polydispersity index, zeta potential, viscosity, spreadability, and in vitro diffusion. The results confirmed acceptable nanoscale particle size, and stable zeta potential values. In vitro drug release studies demonstrated that certain formulations achieved rapid release, while others exhibited sustained release patterns, depending on the type and concentration of gelling agent. Overall, the study highlights that Orphenadrine-loaded nanogels based on Carbopol 940 and HPMC provide stable physical attributes, good spreadability, and desirable release behavior, suggesting their potential as effective carriers for topical drug delivery.

INTRODUCTION

Drug delivery has been a cornerstone of medical practice since ancient times, evolving continuously to improve therapeutic efficacy and patient compliance. In ancient systems of medicine, drug delivery relied primarily on crude formulations such as decoctions, tinctures, ointments, and poultices prepared from plant extracts and minerals. These systems, though effective to a certain extent, faced limitations such as poor stability, lack of controlled release, low

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bioavailability, and difficulties in targeting specific sites of action.[1] In contrast, modern nanotechnology-based drug delivery systems, particularly nanogels, represent a paradigm shift. By incorporating drugs into nanoscale carriers, these systems offer enhanced solubility, targeted delivery, sustained release, and improved therapeutic efficiency. The ability of nanogels to cross biological barriers, provide site-specific action, and reduce systemic side effects marks a significant advancement compared to ancient topical or oral dosage forms[2-3].

Nanogels are nano-sized hydrogel particles formed by cross-linked polymer networks that possess high water content, biocompatibility, and tunable properties. Their nanoscale dimensions allow them to interact effectively with biological membranes, while their porous structure facilitates encapsulation of diverse drugs. They exhibit advantages such as stimuli responsiveness, high drug-loading capacity, stability, and patient-friendly application, making them suitable for multiple routes of administration including topical, oral, ocular, and parenteral delivery[4].

Existing studies have widely reported the development of nanogels for non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics, antifungals, and phytoconstituents, demonstrating improved permeation and therapeutic efficacy compared to conventional gels[5-7]. For instance, Tenoxicam nanogels developed with Noveon polymer displayed prolonged anti-inflammatory activity, while silver nanoparticle-loaded phytoconstituent nanogels enhanced antimicrobial properties. Similarly, celecoxib-based nanogels achieved superior drug release and stability compared to traditional formulations[5-7].

In comparison, the present study focuses on the formulation and evaluation of Orphenadrine-loaded nanogels using Carbopol 940 and HPMC polymers. Unlike earlier reports that largely centered on anti-inflammatory or antimicrobial drugs, this study explores Orphenadrine—a centrally acting muscle relaxant—delivered through a nanogel platform for the first time. The novelty lies in combining Carbopol and HPMC for optimal gel consistency and stability, while systematically evaluating particle size, polydispersity index, zeta potential, viscosity, spreadability, and in vitro drug release profiles. This comprehensive evaluation ensures not only formulation stability but also improved bioavailability and therapeutic performance, distinguishing it from existing nanogel studies.

Therefore, this work bridges the gap between ancient semisolid drug carriers and modern nanotechnology-based systems, highlighting how nanogels offer a superior alternative with controlled release, targeted delivery, and patient-friendly application. It also establishes the unique application of nanogel technology for Orphenadrine delivery, setting a foundation for future clinical and industrial translation.

MATERIALS AND METHODS:

Determining λmax and constructing a calibration curve:

The instruments used in the study were as follows: a UV/Visible Spectrophotometer 1800 series from Shimadzu and a Digital analytical balance from Saartorius, India. To determine the λmax, a 1 µg/mL solution of Orphenadrine was prepared and scanned in spectrum mode across the range of 200–400 nm.

Construction of calibration curve:

Stock preparation:100mg of Orphenadrine was added to a 100 mL volumetric flask. The drug was

dissolved in Methanol, and the volume was made up to the mark with Methanol.

Standard preparation: 5 mL of stock solution was pipetted out into a 50 mL volumetric flask, and the volume was made up to the mark with Methanol.

Working standard preparation: 0.2, 0.4, 0.6, 0.8, 1.0, and 1.2 mL were pipetted out into a 10 mL volumetric flask to obtain the concentration of 2 to 12 µg/mL.

Absorbance of working standard solutions was recorded, and a calibration curve was plotted at the determined λmax of 202 nm.[8]

FORMULATION OF ORPHENADRINE NANOGEL:

Preparation of Carbopol 940 and HPMC Gel Bases

Carbopol 940 and HPMC gels were formulated at concentrations of 0.5%, 1%, and 2% w/v. For the preparation of Carbopol 940 gels**,** accurately weighed quantities of Carbopol 940 (100, 200, and 400 mg) were gradually dispersed in 15–18 mL of distilled water with continuous stirring to prevent agglomeration. The dispersion was allowed to stand for 30–60 minutes to ensure complete hydration, and the final volume was adjusted to 20 mL with distilled water. For the preparation of HPMC gels**,** accurately weighed quantities of HPMC (100, 200, and 400 mg) were dispersed in approximately one-third of the required volume (5–7 mL) of hot distilled water (80–90°C) under constant stirring. The remaining volume of water was then added to make up to 20 mL, followed by stirring until a uniform mixture was obtained. The dispersion was left undisturbed for several hours (or overnight) to facilitate complete hydration and gel formation.

Table 1: Formulation Table of Carbopol 940 and HPMC Gels (0.5%, 1%, and 2% w/v)

Material	F_G1	F_G2	F_G3	F_G4	F_G5	F_G6
Carbapol(mg)	100 (0.5%)	200 (1%)	400 (2%)	-	-	-
HPMC(mg)	-	-	-	100 (0.5%)	200 (1%)	400 (2%)

Formulation of Orphenadrine Nanoparticles and Gel Incorporation

Nanoparticles were prepared using the solvent evaporation method. For F1, 500 mg of Orphenadrine was dissolved in 10 mL of methanol, and 700 mg of Eudragit S-100 was dissolved in 25 mL of acetone, without any surfactant. For F2 and F4**,** Span 80 (1 mL for F2, 2 mL for F4) was added to the Eudragit solution. For F3 and F5**,** Tween 80 (1 mL for F3, 2 mL for F5) was added, as indicated in Table 1. The drug and polymer solutions for each formulation were combined to form a precipitate, followed by the addition of 250 mL of distilled water. Each mixture was homogenized at 2000 rpm for 3 hours to obtain a suspension of reduced particle size, then centrifuged at 1000 rpm for 15 minutes. The residue was collected, dried, and continuously mixed to yield nanoparticles, which were stored in a closed container. Approximately 1 g of nanoparticles was obtained from each formulation.[9]

Table 2: Composition of Orphenadrine Nanoparticle Formulations (F1–F5)

Material	F1	F2	F3	F4	F5
Orphenadrine(mg)	500	500	500	500	500
Eudragit(mg)	700	700	700	700	700
SPAN 80(ml)	-	1	-	2	-
TWEEN 80(ml)	-	-	1	-	2

Incorporation of Nanoparticles into Gel Bases

The nanoparticles exhibiting the best particle size (F3) were incorporated into the previously prepared gel bases. Each gel formulation (F^G1–

F^G6)(20ml) received the F3 nanoparticles(1gram) to produce nanoparticle-loaded gels for further evaluation.

Table 3: Incorporation of F3 Nanoparticles into Gel Bases

Gel Formulation	Gel Base Type	Gel Concentration	Nanoparticles Added
F^G1	Carbopol 940	0.5% w/v	F3
F^G2	Carbopol 940	1% w/v	F3
F^G3	Carbopol 940	2% w/v	F3
F^G4	HPMC	0.5% w/v	F3
F^G5	HPMC	1% w/v	F3
F^G6	HPMC	2% w/v	F3

EVALUATION OF ORPHENADRINE NANOGEL:

Particle Size:

Particle Size determines stability, drug release, and bioavailability of nanoparticles. Smaller particles enhance surface area, dissolution, and membrane permeation, making size optimization essential.

Zeta Potential:

Zeta Potential indicates nanoparticle surface charge, influencing colloidal stability and biological interactions. High values prevent aggregation and aid in predicting cellular uptake.

Viscosity:

Viscosity governs the rheological behavior of gels, affecting spreadability, drug diffusion, and patient compliance. Optimal viscosity ensures ease of application and controlled release.

Polydispersity Index:

Polydispersity Index (PDI) reflects particle size uniformity. Low values indicate homogeneity and stability, while high values suggest variability that may affect formulation quality.[10]

The particle size, zeta potential, viscosity, and polydispersity index of the prepared formulations were analyzed using a Zetasizer Nano ZS90 (Malvern Instruments, UK; version 7.1)**.** Samples were suitably diluted (1:100, v/v) with distilled water to avoid multiple scattering effects and allowed to equilibrate for 30 minutes prior to measurement. The instrument is capable of detecting particles in the range of 1–6000 nm. These parameters provided insights into the stability, uniformity, and nanoscale characteristics of the formulations.

Spreadability:

Spreadability is an important characteristic of semisolid formulations such as gels and creams, as it reflects the ease with which the product can be applied uniformly over the affected area. Good spreadability ensures better patient compliance, accurate dosing, and effective therapeutic action by allowing the drug to be evenly distributed across the site of application. It is directly influenced by the viscosity and consistency of the formulation.

Approximately 1 g of gel was sandwiched between two glass slides, and a 250 g weight was gently placed on the upper slide to form a thin, uniform film. The time required for the upper slide to move

apart from the lower one was recorded, and spreadability (S) was calculated using the formula:

$$S = \frac{M \times L}{T}$$

M = Weight applied.

L = Length of glass slide.

T = time (seconds) taken to separate the slides.

In vitro drug diffusion studies:

In vitro drug release studies are performed to evaluate the rate and extent of drug diffusion from a formulation into a suitable medium, simulating in vivo conditions. These studies provide critical insights into the release kinetics, mechanism of drug transport, and expected therapeutic performance. Dialysis membrane or diffusion cell methods are commonly employed, and results help in predicting in vivo bioavailability and optimizing formulation design. [11]

In vitro drug diffusion was evaluated using dialysis method. The mean (n=3). Known quantity of nanogel (1 g) was loaded into an egg membrane containing 1 mL of phosphate buffer (pH 7.4). The sealed membrane was immersed in 200 mL of the same buffer maintained at 37 ± 0.5°C under constant stirring at 100 rpm using a magnetic stirrer. At predetermined intervals, 3 mL samples were withdrawn and immediately replaced with fresh buffer to maintain sink conditions. The samples were suitably diluted and analyzed spectrophotometrically to quantify the amount of drug released.

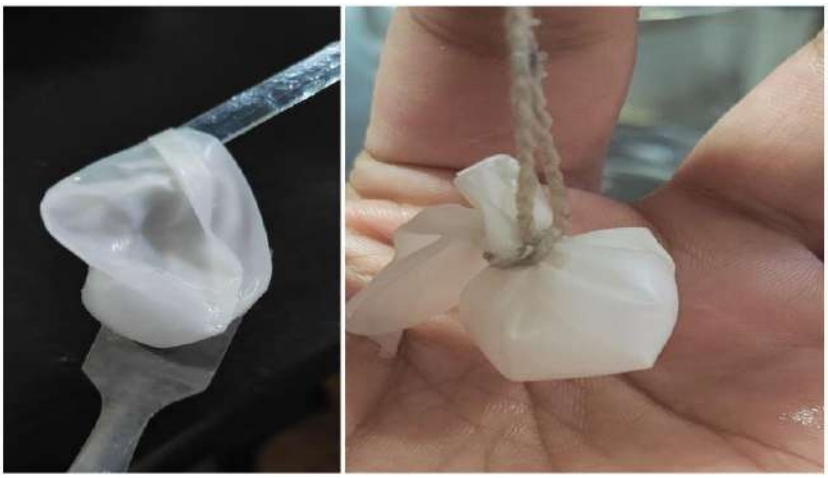

Fig 1: Diffusion study by egg membrane

RESULTS AND DISCUSSION:

Determination of λ max by UV spectrophotometer:

The lambda max was found to be 202.00nm

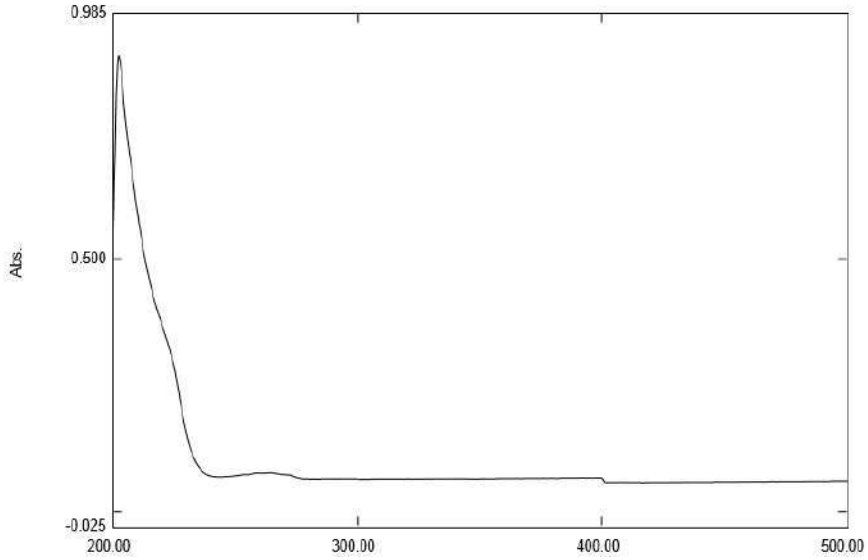

Fig 2: Spectrum of Orphenadrine

Construction of calibration curve by UV spectrophotometry:

The λmax of Orphenadrine was determined to be 202 nm, with a linearity (R^2) value of 0.9983

Table 4: Calibration curve values[n=3]

S. No	Conc(ppm)	Absorbance (Mean±SD)
1	2ppm	0.224±0.010
2	4ppm	0.333±0.021
3	6ppm	0.438±0.028
4	8ppm	0.552±0.022
5	10ppm	0.638±0.031

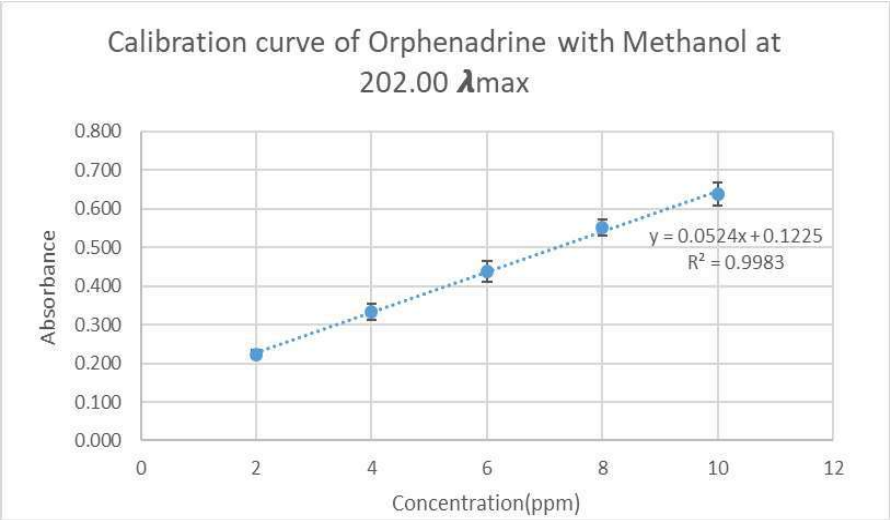

Fig 3: Calibration curve of Orphenadrine [n=3]

Determination of Particle size and Particle size distribution (Polydispersity index):

Particle size and viscosity were found to be 189.83nm and 0.8872 cP, respectively.

Determination of Zeta potential and Viscosity:

Zeta potential and viscosity were found to be -27.6mV and 0.8872 cP, respectively.

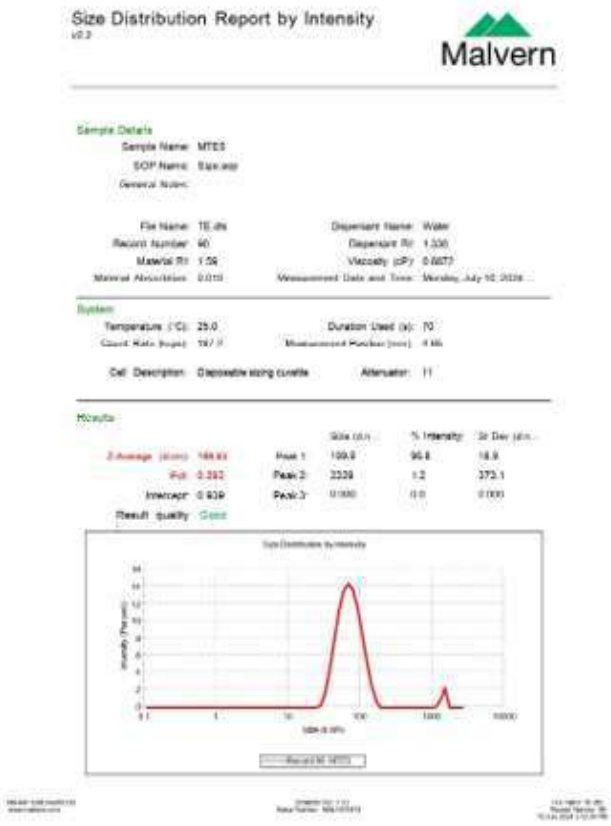

Fig4: Data of Particle size and PDI

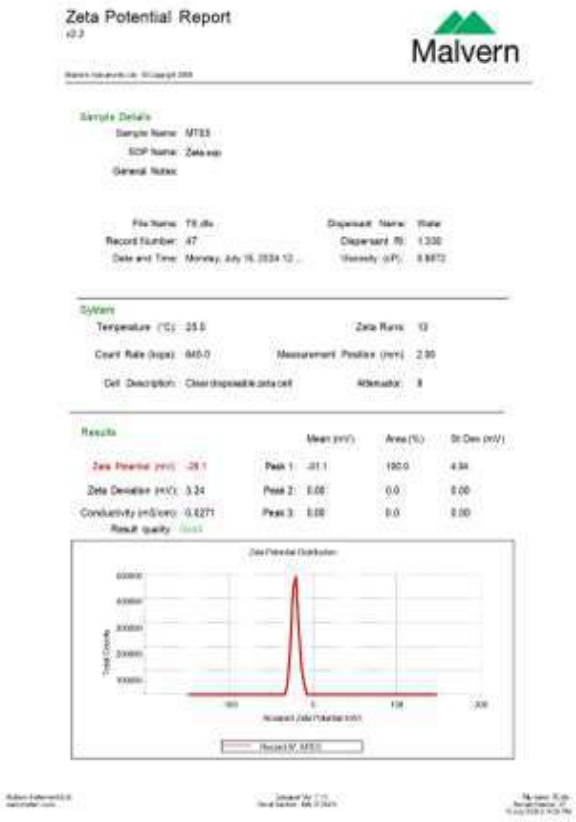

Fig5: Zeta potential and Viscosity

Spredability:

Spreability test was performed and found to be 5.2 g.cm/s

Drug release studies:

Formulation F_G1 has release the drug quickly, 100% in 75 minutes.

Table 5: Data of diffusion studies [n=3]

S.No	Time (min)	F_G1 (Carbapol 0.5 %)	F_G2 (Carbapol 1 %)	F_G3 (Carbapol 2 %)	F_G4 (HPMC 0.5 %)	F_G5 (HPMC 1 %)	F_G6 (HPMC 2 %)
1.	5 min	8.67 ±0.2	6.2±0.3	3.34±0.4	6.25±0.1	4.14±0.2	2.48±0.2
2.	10 min	17.82±0.3	8.58±0.1	6.12±0.2	14.97±0.3	7.88±0.2	4.12±0.5
3.	15 min	28.73±0.1	20.13±0.3	13.44±0.5	22.76±0.1	16.34±0.1	7.44±0.3
4.	30 min	45.11±0.2	38.47±0.2	22.12±0.1	41.87±0.3	28.11±0.2	15.1±0.6
5.	45 min	67.39±0.4	50.84±0.5	33.16±0.2	57.88±0.2	42.52±0.2	24.1±0.4
6.	60 min	87.14±0.7	65.91±0.6	48.8±0.9	74.73±0.5	55.83±0.4	36.8±0.8

7.	75 min	100±1.2	75.22±1	60.4±0.3	86.82±0.6	64.41±0.5	48.4±0.5
8.	90 min	100±1.1	87.23±1.2	73.6±0.3	99.02±0.9	78.6±0.3	63.6±0.4
9.	120 min	100±0.8	98.88±0.6	88.6±0.2	100±0.2	90.6±0.6	70.6±1.1

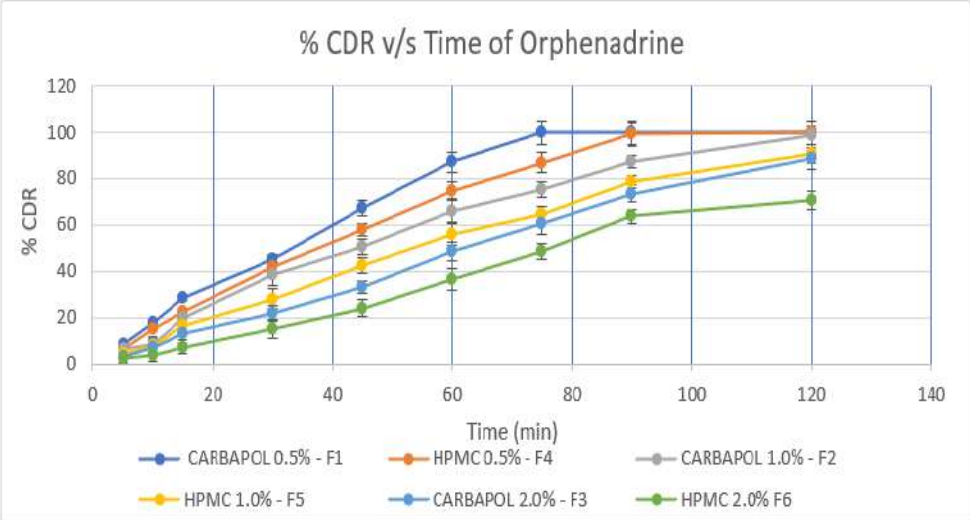

Fig 6: % CDR of Orphenadrine in 7.4 Phospthate buffer [n=3]

CONCLUSION:

In this study, Orphenadrine-loaded nanoparticles were successfully prepared using the solvent evaporation method, with careful optimization of surfactant type and concentration. Among the formulations, F3 exhibited the smallest particle size, demonstrating superior nanoscale characteristics suitable for incorporation into polymeric gels. Carbopol 940 and HPMC gels were prepared at varying concentrations (0.5%, 1%, and 2% w/v), and the optimized nanoparticles were effectively incorporated into these gels to form nanogel formulations. The resulting nanoparticle-loaded gels showed good homogeneity and stability. The nanogels were evaluated for particle size, polydispersity index (PDI), zeta potential, viscosity, Spreadability, and in vitro drug release. In vitro diffusion studies using the dialysis technique revealed controlled and sustained release of Orphenadrine across the membrane, highlighting the potential of the nanogel system to enhance drug delivery. Formulations with rapid release (100% in ≤90 min) suggest that the drug is quickly available, due to lower viscosity and weaker gel-network interactions. The λmax of the drug was determined to be 202 nm, with excellent linearity (R^2 = 0.9983), confirming the reliability of the analytical method. Overall, the study demonstrates that nanoparticle-loaded Carbopol and HPMC gels can serve as a promising platform for achieving improved bioavailability, sustained release, and therapeutic efficacy of Orphenadrine. These findings provide a strong foundation for further preclinical and clinical investigations into polymeric nanogel-based drug delivery systems.

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