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DEVELOPMENT OF SUSTAINED RELEASE TABLETS OF HYDROXYCHLOROQUINE AND TINOSPORA CORDIFOLIA STEM EXTRACT FOR RHEUMATOID ARTHRITIS

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Abstract:

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disorder characterized by persistent synovial inflammation, joint pain, stiffness, and progressive disability. Hydroxychloroquine is a widely used disease-modifying antirheumatic drug (DMARD) that helps control disease progression, while *Tinospora cordifolia* stem extract possesses significant anti-inflammatory, antioxidant, and immunomodulatory properties. The present study aimed to develop and evaluate sustained-release tablets containing Hydroxychloroquine and *Tinospora cordifolia* stem extract for improved management of rheumatoid arthritis. Sustained-release formulations were prepared using suitable release-retarding polymers to provide prolonged drug release and reduce dosing frequency. The tablets were evaluated for pre-compression and post-compression parameters, including flow properties, hardness, friability, weight variation, drug content, and in vitro dissolution studies. The optimized formulation exhibited satisfactory physicochemical characteristics and sustained drug-release behavior over an extended period. The developed sustained-release tablet may improve patient compliance, maintain therapeutic drug levels, and enhance the long-term treatment of rheumatoid arthritis through the combined therapeutic benefits of Hydroxychloroquine and *Tinospora cordifolia.*

Keywords: Rheumatoid Arthritis, Hydroxychloroquine, *Tinospora cordifolia*, Sustained-Release Tablets, Controlled Drug Delivery, Disease-Modifying Antirheumatic Drug (DMARD), Anti-inflammatory Activity.

INTRODUCTION:

Rheumatoid arthritis is a chronic, systemic, autoimmune inflammatory disorder that primarily affects synovial joints, leading to persistent synovitis, progressive cartilage destruction, and bone erosion. It is characterized by symmetrical joint involvement, morning stiffness, swelling, pain, and progressive loss of function. The global prevalence of RA is estimated to be around 0.5–1% of the population, with a higher incidence in women than men, particularly between the ages of 30–50 years [1]. Although the exact etiology of RA is not fully understood, it is believed to result from a complex interplay of genetic predisposition, environmental triggers, and immune dysregulation. Pathophysiologically RA involves the activation of T cells, B cells, and macrophages, which release pro-inflammatory cytokines such as tumor necrosis factoralpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6) [2]. These mediators promote synovial hyperplasia, pannus formation, angiogenesis, and degradation of cartilage and bone ultimately resulting in joint deformities and disability [3].

Sustained release drug delivery systems are designed to maintain steady plasma drug concentrations within the therapeutic window for a prolonged duration, enhancing drug effectiveness while minimizing toxicity and adverse effects [4]. These systems work by employing various release-controlling mechanisms, such as diffusion, dissolution, osmosis, and erosion, to regulate the rate at which the drug is released into the systemic circulation [5]. The need for SR formulations arises particularly in the treatment of chronic diseases such as hypertension, diabetes, cardiovascular diseases, and neurological disorders, where consistent drug levels are crucial for maintaining optimal therapeutic outcomes [6].SR drug delivery systems have gained significant attention in the pharmaceutical industry due to their ability to maintain steady drug levels over an extended period, improving patient compliance and therapeutic efficacy. These systems are designed to release the drug at a predetermined rate, minimizing fluctuations in plasma drug concentration [7].

Hydroxychloroquine (HCQ) is a synthetic 4-aminoquinoline derivative originally developed as an antimalarial agent and later widely adopted for the treatment of autoimmune and inflammatory disorders such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) due to its immunomodulatory properties and favorable safety profile compared to chloroquine [8,9]. Over time, hydroxychloroquine has become an important conventional DMARD, particularly in long-term management strategies for autoimmune diseases [11]. The pharmacological activity of hydroxychloroquine involves multiple mechanisms of action. It accumulates within lysosomes, increasing intracellular pH and thereby interfering with antigen processing and presentation [12]. Additionally, hydroxychloroquine inhibits toll-like receptor (TLR) signaling pathways, leading to reduced activation of dendritic cells and decreased production of pro-inflammatory cytokines, which contributes to its anti-inflammatory and immunomodulatory effects [8,10]. These mechanisms are particularly beneficial in controlling autoimmune responses and reducing disease progression in rheumatoid arthritis.

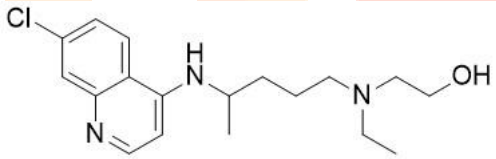


Fig No. 1 Structure of Hydroxychloroquine

Tinospora cordifolia (Willd.) Hook. f. & Thomson, commonly known as Guduchi, is an important medicinal plant of the family Menispermaceae widely used in traditional Ayurvedic medicine [13]. The stem of *T. cordifolia* contains bioactive constituents including alkaloids, diterpenoid lactones, glycosides, steroids, and polysaccharides that contribute to its anti-inflammatory, antioxidant, and immunomodulatory properties [14]. Experimental studies have demonstrated that *T. cordifolia* extract suppresses arthritic inflammation and reduces the production of pro-inflammatory cytokines such as TNF-α, IL-1β, IL-6, and IL-17, thereby limiting joint and bone damage associated with RA [15]. These findings suggest that T. cordifolia may serve as a promising natural therapeutic agent for the management of rheumatoid arthritis and may enhance the efficacy of conventional antirheumatic therapy [16].

Fig No. 2 Stem of Tinospora cordifolia

MATERIAL AND METHODS:

Collection and Authentication of Plant:

The Stem of the plant *Tinospora cordifolia* were collected from Chail Chowk, Mandi (H.P), in the month of September, 2025. The plant was then authenticated by the Dr. Ved Prakash Assistant Professor Botany Govt. College Bassa, Gohar, Mandi (H.P).

Extraction Of Plant Extract (Soxhlet extraction):

Procedure:

Step-I: Preparation of Plant Material-Collect the plant and wash thoroughly with the water. Shade dries for the weeks and then grind into coarse powder (465.4g).

Step- II: Loading the Sample-Weigh specific quantity of powdered plant and packed into the thimble (60g in each thimble). Placed the thimble in Soxhlet extractor, attached the extractor to the round bottom flask containing solvent.

Step-III: Extraction Process-Gently heat the solvent in the round-bottom flask. The solvent evaporates and moves upward through the Soxhlet apparatus. It then condenses in the condenser and drips onto the thimble containing the plant material. Once the chamber fills up, the solvent siphons back into the round-bottom flask with the extracted compounds. This repeated cycle of evaporation, condensation, and siphoning continues for several time until the solvent in the siphon turns nearly colourless, showing that the extraction process is complete.

Step-IV: Extract Recovery-Once the extraction process is finished, the round bottom flask is removed from the assembly and extracted compounds are collected. The solvent is removed to obtain concentrated extract and stored in desiccator [17].

Phytochemical Screening:

Preliminary phytochemical screening of *Tinospora cordifolia* stem extract revealed the presence of various bioactive constituents, including alkaloids, glycosides, flavonoids, phenolic compounds, terpenoids, steroids, and polysaccharides. These phytochemicals are reported to possess anti-inflammatory, antioxidant, and immunomodulatory activities, which contribute to the therapeutic potential of Tinospora cordifolia in the management of rheumatoid arthritis and other inflammatory disorders [18].

Characterization of Hydroxychloroquine

Hydroxychloroquine was evaluated for its physical appearance, melting point, solubility profile, and identification characteristics according to pharmacopeial standards.

DESIGNING OF FORMULATION:

Wet granulation method: Accurately weighed quantities of Hydroxychloroquine, Tinospora cordifolia extract, HPMC K100M, Ethyl Cellulose, Guar Gum, and Microcrystalline Cellulose (MCC) were passed through sieve No. 40 and mixed uniformly in a mortar for 10–15 minutes. Polyvinylpyrrolidone (PVP K30) was dissolved in a suitable quantity of purified water to prepare the binder solution. The binder solution was gradually added to the powder blend with continuous mixing until a coherent wet mass was obtained.

The wet mass was passed through sieve No. 16 to produce granules and dried in a hot air oven at 50–60°C until the desired moisture content was achieved. The dried granules were then passed through sieve No. 20 to obtain uniform-sized granules. Finally, talc and magnesium stearate were added as glidant and lubricant, respectively, and blended thoroughly with the granules.

EVALUATION PARAMETERS OF POWDER BLEND:

The blend of powders was evaluated for the following parameters:

Angle of Repose:

The fixed funnel method was used to calculate the angle of repose. The granules were permitted to pass through a funnel that was set on a level surface at a specific height. The angle of repose was computed using the following formula after the height (h) and radius (r) of the powder heap were measured [19].

$$\theta = \tan^{-1}(h/r)$$

Where: h = height of pile, r = radius of pile

Bulk Density:

A precisely measured amount of granules was added to the measuring cylinder, and the initial volume was recorded [20].

$$\text{Bulk Density} = \text{Mass of powder} / \text{Bulk volume}$$

Tapped Density:

The granule-filled measuring cylinder was mechanically tapped until a consistent volume was achieved, at which point the final tapped volume was noted [21].

$$\text{Tapped Density} = \text{Mass of powder} / \text{Tapped volume}$$

Carr's Compressibility Index:

Granules were precisely weighed and then put into a dry, clean measuring cylinder. Bulk volume was defined as the initial volume that the granules occupied. After that, the cylinder was mechanically tapped a certain number of times to achieve a consistent volume; the resulting volume was recorded as the tapped volume. Carr's compressibility index was computed using bulk density and tapped density [19].

$$\text{Carr's Index} = \text{Tapped Density} - \text{Bulk Density} / \text{tapped Density} * 100$$

Formulation of Tablet:

The sustained-release tablets containing Hydroxychloroquine and Tinospora cordifolia stem extract were prepared by the wet granulation method according to the composition shown in Table 1. Each formulation contained 200 mg of Hydroxychloroquine and 100 mg of Tinospora cordifolia stem extract, while the concentrations of HPMC K100M, Ethyl Cellulose, and Guar Gum were varied to optimize the drug-release profile. Hydroxychloroquine, Tinospora cordifolia extract, HPMC K100M, Ethyl Cellulose, Guar Gum, and Microcrystalline Cellulose (MCC) were accurately weighed, passed through sieve No. 40, and blended thoroughly to obtain a uniform powder mixture. Polyvinylpyrrolidone K30 (PVP K30) was used as a binder to prepare the wet mass, which was subsequently granulated through sieve No. 16 and dried in a hot air oven at 50–60°C. The dried granules were resized through sieve No. 20 and lubricated with talc and magnesium stearate. The lubricated granules were then compressed into tablets using a rotary tablet compression machine fitted with a 9.7 mm punch and die set. A total of six formulations (F1–F6) were prepared and evaluated for their physicochemical characteristics and sustained-release performance.

Table no.1 Composition of Unit Dose of Tablet

Sr NO.	Chemicals	F1	F2	F3	F4	F5	F6
1	Hydroxychloroquine	200mg	200mg	200mg	200mg	200mg	200mg
2	Extract	100mg	100mg	100mg	100mg	100mg	100mg
3	HPMC K100	100mg	80mg	60mg	80mg	60mg	40mg
4	Ethyl Cellulose	40mg	40mg	40mg	20mg	20mg	20mg
5	Guar Gum	60mg	80mg	100mg	100mg	120mg	140mg
6	MCC	65mg	65mg	65mg	65mg	65mg	65mg
7	PVP K30	20mg	20mg	20mg	20mg	20mg	20mg
8	Talc	10mg	10mg	10mg	10mg	10mg	10mg
9	Magnesium Stearate	5mg	5mg	5mg	5mg	5mg	5mg

Post-compression Evaluation of Tablets:

The quality and effectiveness of the manufactured herbal tablets were assessed by post-compression evaluation experiments.

Physical Appearance: The general appearance of tablet was studies visually in shape, color, texture and odor.

Thickness Test: A Vernier caliper was used to measure the tablet thickness. The average thickness was determined using tablets that were chosen at random [22].

Hardness Test: A Monsanto hardness tester was used to measure the tablets' hardness. The average hardness of randomly chosen tablets was measured in kg/cm² [114].

Friability Test: The Roche friabilator was used to conduct the friability test. The friabilator was used to rotate pre-weighed tablets at 25 RPM for four minutes. After the test was finished, the tablets were dedusted and reweighed [23].

Friability (%) =initial weight –final weight /initial weight *100

Weight Variation Test: A digital balance was used to weigh each of the twenty tablets that were chosen at random. In accordance with pharmacopoeial norms, the average weight was computed and contrasted with the weights of individual tablets [24].

Disintegration Test: USP disintegration equipment was used to conduct the disintegration test. The time it took for the tablets to completely disintegrate was noted after they were put in a basket rack assembly with distilled water kept at 37 ± 2°C [25].

Dissolution study: Using USP dissolution equipment with an appropriate dissolution medium kept at 37 ± 0.5°C, an in vitro dissolution investigation was conducted. Samples were taken out at prearranged intervals and subjected to spectrophotometric analysis [22].

Drug Release (%) =Amount of drug released/Total amount of drug *100

Results and Discussion:

Charecterization of Hydroxychloroquine:

Physical Appearance:

Table No.2 Physical properties of Hydroxychloroquine

Parameter	Observations
Texture	Crystalline powder
Color	White to partially white
Taste	Intensely bitter
Odor	Odorless

Melting Point: Melting Point of HCQ was found to be 91 by using Digital Melting/Boiling point apparatus.

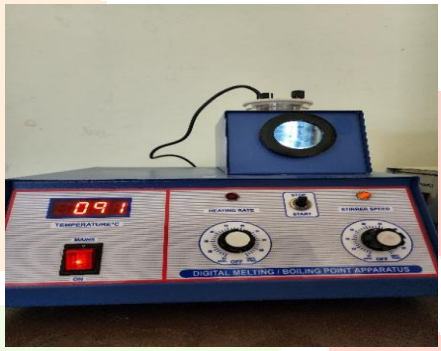


Fig. No. 1 Melting Point of HCQ

Solubility Profile:

Hydroxychloroquine sulfate exhibits the following solubility characteristics:

Table No. 3 Solubility Profile of Hydroxychloroquine

Solvent	Solubility
Water	Freely Soluble
Methanol	Soluble
Etthanol (95%)	Slightly Soluble
Chloroform	Practically Insoluble
Ether	Practically Insoluble

UV Spectroscopy:

Ultraviolet spectroscopic analysis of Hydroxychloroquine was performed in the wavelength range of 200–800 nm. HCQ exhibits characteristic absorption maxima at approximately 343 nm in suitable solvent (i.e Water).

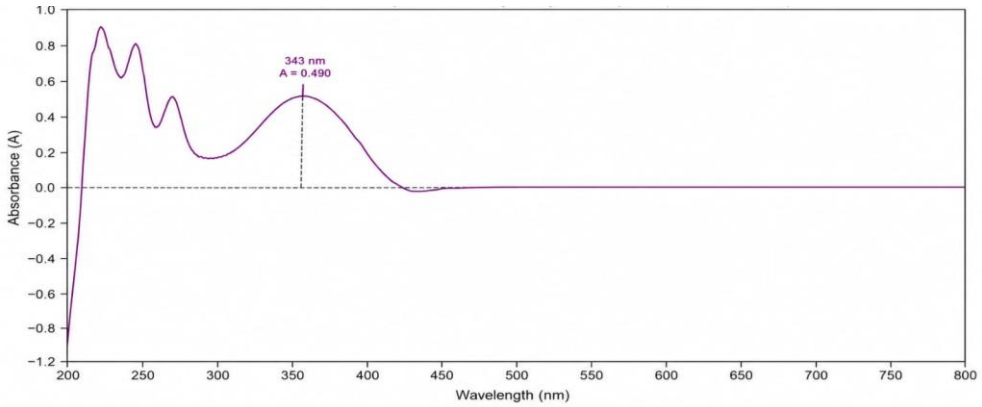


Fig. 1 Absorbance of HCQ in UV Spectrophotometer

HPLC:

HPLC analysis of Hydroxychloroquine was carried out using UV detection at 343 nm. The chromatogram showed a sharp and well-defined peak at a retention time of 1.95 min, corresponding to HCQ. The absence of significant interfering peaks near the drug retention time indicated good specificity of the method. The observed retention time and peak characteristics confirmed the identity of HCQ and demonstrated the suitability of the drug sample for further formulation studies.

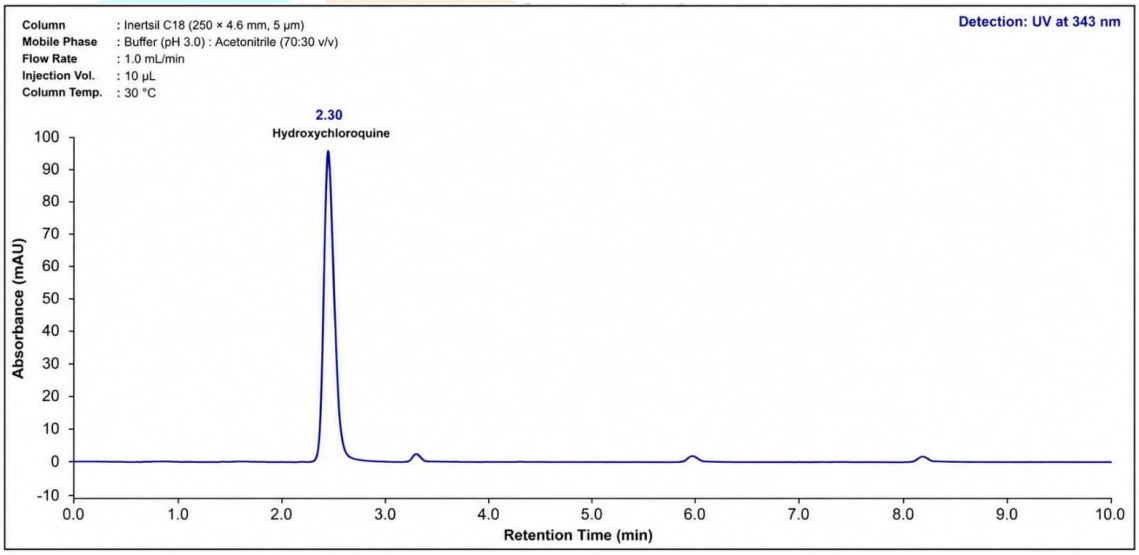


Fig. 6.6 HPLC Chromatogram of HCQ

Percentage Yield:

The percentage yield of *Tinospora cordifolia* stem extract was determined after the extraction process. From 465.4 g of dried stem powder, 65 g of dried extract was obtained, resulting in a percentage yield of 13.97% w/w.

The yield was calculated using the ratio of the weight of dried extract to the weight of dried powder and was found to be satisfactory for further formulation and evaluation studies.

Phytochemical Screening:

Table No.4 Qualitative analysis of *Tinospora cordifolia* stem extract in Ethanol

Sr. No.	Phytochemicals	Phytochemical Test	Result
1.	Alkaloids	Dragendorff's Test	+
2.	Terpenoids	Salkowski Test	+
3.	Flavanoid	Shinoda Test	+
4.	Tannin	Ferric Chloride Test	+
5.	Steroids	Liebermann–Burchard Test	+
6.	Carbohydrates	Fehling's Test	-
7.	Glycosides	Keller-Killani Test	+
8.	Amino acids	Ninhydrin Test	+

(+) =Present

(-) = Absent

Pre-compression Parameters of Tablet:

The pre-compression parameters of the prepared granules were evaluated to determine their flow and compression characteristics, and the results are presented in Table 2. The angle of repose of all formulations ranged from 27.26 ± 0.34° to 30.42 ± 0.25°, indicating good to excellent flow properties. Among the formulations, F4 exhibited the lowest angle of repose (27.26 ± 0.34°), suggesting excellent flow behavior, whereas F6 showed the highest value (30.42 ± 0.25°), which still indicated acceptable flow characteristics. The bulk density of the granules was found to be in the range of 0.463 ± 0.012 to 0.558 ± 0.013 g/mL, with formulation F5 showing the highest bulk density. The tapped density ranged from 0.551 ± 0.013 to 0.628 ± 0.012 g/mL, indicating uniform packing ability of the granules. The Carr's Compressibility Index was observed between 11.15 ± 0.18% and 16.12 ± 0.28%. Formulation F5 exhibited the lowest compressibility index, indicating excellent flowability, whereas F1 showed the highest value but remained within acceptable limits. The Hausner ratio ranged from 1.13 ± 0.01 to 1.19 ± 0.01, confirming good flow properties of all formulations. Overall, the pre-compression results demonstrated that the granules possessed satisfactory flow and compressibility characteristics suitable for tablet compression.

Table No. 5 Pre compression evaluation parameters of formulations F1-F6

Parameter	F1	F2	F3	F4	F5	F6
Angle of Repose (°)	28.42 ± 0.25	30.15 ± 0.31	29.27 ± 0.28	27.26 ± 0.34	28.32 ± 0.26	30.42 ± 0.25
Bulk Density (g/mL)	0.463 ± 0.012	0.487 ± 0.015	0.471 ± 0.011	0.526 ± 0.014	0.558 ± 0.013	0.514 ± 0.016
Tapped Density (g/mL)	0.552 ± 0.014	0.565 ± 0.017	0.551 ± 0.013	0.598 ± 0.016	0.628 ± 0.012	0.604 ± 0.018
Carr's Index (%)	16.12 ± 0.28	13.81 ± 0.32	14.52 ± 0.25	12.04 ± 0.21	11.15 ± 0.18	14.90 ± 0.27
Hausner Ratio	1.19 ± 0.01	1.16 ± 0.02	1.17 ± 0.01	1.14 ± 0.01	1.13 ± 0.01	1.18 ± 0.02

Evaluation of Prepared Tablet:

The prepared sustained-release tablets were evaluated for various post-compression parameters, including diameter, thickness, weight variation, hardness, friability, and disintegration time. The results are presented in Table 6. All formulations were circular, uniform in appearance, and free from visible defects such as cracks, chipping, or discoloration. The diameter of all tablet formulations was found to be approximately 9.00 mm, indicating uniform die filling during compression. The thickness ranged from 5.12 ± 0.02 mm to 5.28 ± 0.04 mm, showing minimal variation among the formulations.

The average tablet weight varied from 597.8 ± 4.5 mg to 602.1 ± 4.7 mg and complied with pharmacopeial limits for weight variation. Tablet hardness was found to be in the range of 9.18 ± 0.16 to 14.12 ± 0.24 kg/cm², indicating adequate mechanical strength to withstand handling, packaging, and transportation. The friability values ranged from 0.52 ± 0.01% to 0.78 ± 0.03%, which were below the acceptable limit of 1%, confirming satisfactory tablet durability. The disintegration time ranged from 3.25 ± 0.08 h to 6.26 ± 0.09 h, demonstrating the influence of polymer concentration on sustaining tablet integrity and drug release. Overall, all formulations exhibited acceptable post-compression characteristics suitable for sustained-release tablet development.

Table No. 6 Results of Post-compression Parameters of Tablet

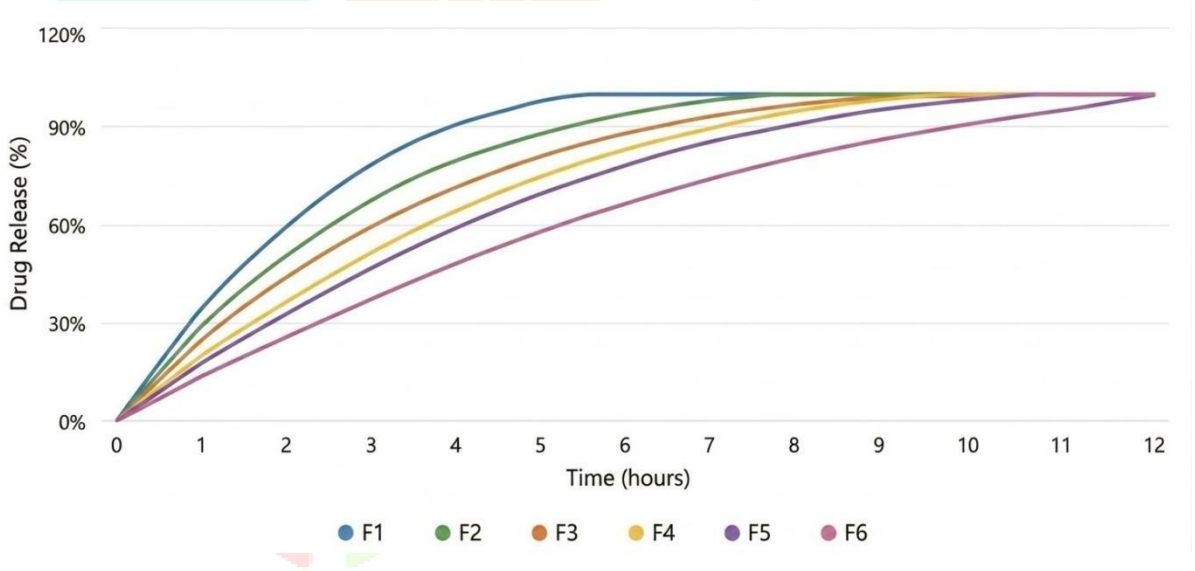
Parameter	F1	F2	F3	F4	F5	F6
Diameter (mm)	9.00 ± 0.01	9.00 ± 0.01	9.00 ± 0.02	9.00 ± 0.01	9.00 ± 0.01	9.00 ± 0.03
Thickness (mm)	5.18 ± 0.04	5.21 ± 0.03	5.25 ± 0.05	5.16 ± 0.03	5.12 ± 0.02	5.28 ± 0.04
Weight Variation (mg)	598.6 ± 4.2	601.3 ± 3.8	597.8 ± 4.5	600.5 ± 3.1	599.9 ± 2.4	602.1 ± 4.7
Hardness (kg/cm²)	9.18 ± 0.16	11.28 ± 0.17	10.16 ± 0.12	12.48 ± 0.18	13.24 ± 0.14	14.12 ± 0.24
Friability (%)	0.78 ± 0.03	0.71 ± 0.02	0.68 ± 0.03	0.61 ± 0.02	0.52 ± 0.01	0.57 ± 0.02
Disintegration Time (h)	3.25 ± 0.08	4.12 ± 0.10	4.44 ± 0.12	5.15 ± 0.11	6.26 ± 0.09	5.32 ± 0.13

The in vitro dissolution study demonstrated a sustained drug release pattern from all formulated batches (F1–F6) in table no.7. Formulation F1 exhibited the fastest release profile, achieving 100% drug release within 6 h. Formulation F2 reached complete drug release at 8 h, whereas formulations F3 and F4 achieved 100% release at 10 h. Formulation F6 showed a more prolonged release pattern and attained complete drug release at 11 h. Among all formulations, F5 exhibited the most sustained release behavior, releasing 99.2% of the drug over a period of 12 h. These findings indicate that increasing the concentration of release-retarding components effectively prolonged the drug release rate. Based on the dissolution profile, formulation F5 demonstrated the most desirable sustained-release characteristics and was considered the optimized formulation for further evaluation.

Table No. 7 Results of dissolution study test of tablets

Sr. No.	Time (h)	F1 (% Drug Release)	F2 (% Drug Release)	F3 (% Drug Release)	F4 (% Drug Release)	F5 (% Drug Release)	F6 (% Drug Release)
1	0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
2	1	36.0 ± 1.2	31.0 ± 1.0	26.0 ± 1.1	20.0 ± 0.9	14.0 ± 0.8	18.0 ± 0.9
3	2	55.0 ± 1.5	48.0 ± 1.4	42.0 ± 1.3	34.0 ± 1.2	24.0 ± 1.0	31.0 ± 1.1
4	3	72.0 ± 1.8	63.0 ± 1.6	56.0 ± 1.5	48.0 ± 1.4	35.0 ± 1.2	44.0 ± 1.3
5	4	86.0 ± 2.0	76.0 ± 1.8	68.0 ± 1.7	61.0 ± 1.5	46.0 ± 1.4	56.0 ± 1.5
6	5	95.0 ± 1.9	85.0 ± 1.8	78.0 ± 1.7	72.0 ± 1.6	56.0 ± 1.5	67.0 ± 1.6
7	6	100.0± 0.0	92.0 ± 1.6	86.0 ± 1.5	81.0 ± 1.4	65.0 ± 1.4	76.0 ± 1.5
8	7	100.0± 0.0	97.0 ± 1.2	92.0 ± 1.3	88.0 ± 1.2	73.0 ± 1.3	84.0 ± 1.2
9	8	100.0± 0.0	100.0± 0.0	96.0 ± 1.1	94.0 ± 1.0	80.0 ± 1.2	90.0 ± 1.1
10	9	100.0± 0.0	100.0± 0.0	99.0 ± 0.8	98.0 ± 0.7	86.0 ± 1.0	95.0 ± 0.9
11	10	100.0± 0.0	100.0± 0.0	100.0± 0.0	100.0± 0.0	91.0 ± 0.9	98.0 ± 0.7
12	11	100.0± 0.0	100.0± 0.0	100.0± 0.0	100.0± 0.0	95.0 ± 0.7	100.0± 0.0
13	12	100.0± 0.0	100.0± 0.0	100.0± 0.0	100.0± 0.0	99.2 ± 0.4	100.0± 0.0

Graph 1. The percentage drug release record mentioned in graph.



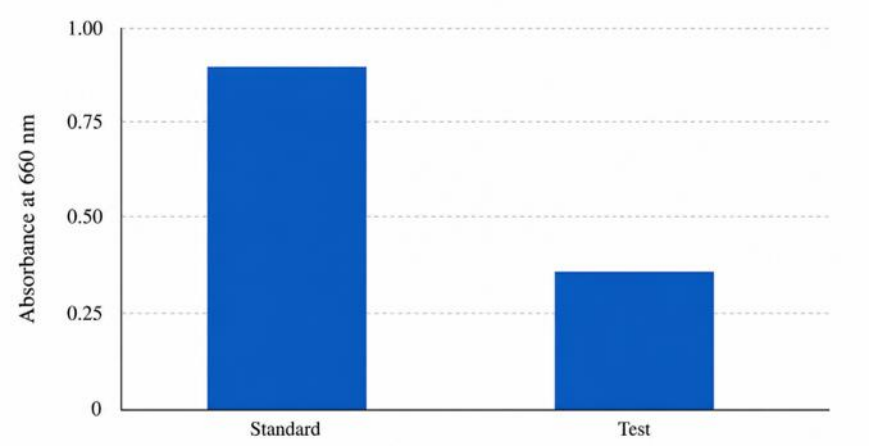
Egg Albumin Denaturation:

The anti-inflammatory activity of the Hydroxychloroquine and *Tinospora cordifolia* tablet was evaluated using the egg albumin denaturation assay. The standard drug showed an absorbance of 0.926, while the test formulation showed an absorbance of 0.368 at 660 nm. The lower absorbance of the test sample indicates inhibition of protein denaturation.

The percentage inhibition was calculated as:

$$\%\text{Inhibition} = 0.926 - 0.368 / 0.926 \times 100 = 60.26\%$$

The test formulation exhibited 60.26% inhibition of protein denaturation, suggesting appreciable anti-inflammatory activity under the experimental conditions. The reduction in absorbance compared with the reference indicates the ability of the formulation to stabilize proteins against heat-induced denaturation, a mechanism associated with anti-inflammatory effects.



Graph No. 3 Absorbance comparison of Standard and test sample

Conclusion:

From the above study, it was concluded that sustained-release tablets containing Hydroxychloroquine and *Tinospora cordifolia* stem extract were successfully formulated using the wet granulation technique. The prepared formulations showed satisfactory pre-compression and post-compression characteristics, including good flowability, compressibility, hardness, friability, weight uniformity, and tablet integrity.

Among all formulations (F1–F6), formulation F5 demonstrated the best overall performance. It exhibited excellent flow properties with the lowest Carr's Index (11.15 ± 0.18%) and Hausner ratio (1.13 ± 0.01), along with acceptable hardness (13.24 ± 0.14 kg/cm²), low friability (0.52 ± 0.01%), and satisfactory weight uniformity.

The in vitro dissolution study showed that F5 provided a controlled and sustained drug-release profile, releasing 99.2% of the drug over 12 hours. The optimized combination of HPMC K100M, Ethyl Cellulose, and Guar Gum effectively controlled drug release while maintaining tablet quality.

The anti-inflammatory activity of the Hydroxychloroquine and *Tinospora cordifolia* tablet was confirmed by the egg albumin denaturation assay. The test formulation showed 60.26% inhibition of protein denaturation, indicating appreciable anti-inflammatory activity and the ability to stabilize proteins against heat-induced denaturation.

The incorporation of *Tinospora cordifolia* stem extract may provide additional anti-inflammatory, antioxidant, and immunomodulatory benefits, enhancing the therapeutic potential of the formulation in rheumatoid arthritis. Therefore, formulation F5 was identified as the optimized sustained-release formulation, with the potential to improve patient compliance, maintain consistent drug levels, and serve as a promising approach for the long-term management of rheumatoid arthritis.

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