RESEARCH PAPER

# Design, Development, and Characterization of Mucoadhesive Buccal Patches Incorporating Diclofenac Diethylamine and Curcumin for Sustained Management of Rheumatoid Arthritis

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**Abstract:**
Rheumatoid arthritis (RA) is a chronic autoimmune joint disorder, and long-term management with oral NSAIDs and DMARDs is still hampered by first-pass metabolism, GI toxicity, and systemic side effects that build up over years of treatment. The buccal route offers a practical workaround, since it bypasses hepatic metabolism and lets a patch be removed instantly if a reaction occurs. This study set out to design and evaluate mucoadhesive buccal patches combining diclofenac diethylamine (DDEA), a fast-acting COX inhibitor, with curcumin, a poorly soluble but broadly anti-inflammatory polyphenol, so that the two could work through complementary mechanisms at lower individual doses. Six HPMC/PVP K30-based formulations (P1–P6) were prepared by solvent casting and assessed for physico-mechanical properties, drug content, and in vitro release. All batches showed consistent weight (252.7 ± 2.2 mg), near-neutral surface pH (6.78 ± 0.04), and strong folding endurance (171 ± 1.8 folds), confirming a reproducible casting process. Formulation P6 performed best overall, releasing 95.6% DDEA and 90.7% curcumin over 8 hours, with drug content of 99.8% and 99.0%, respectively. FTIR and DSC confirmed no significant drug–polymer interaction. Kinetic modelling of P6 pointed to the Higuchi and Korsmeyer–Peppas models as the best fit, indicating a diffusion-driven, non-Fickian release mechanism aided by polymer swelling. Overall, the DDEA–curcumin buccal patch looks like a viable controlled-release alternative to conventional oral RA therapy, though ex vivo permeation, in vivo pharmacokinetic, and stability studies are still needed to establish its clinical potential.

**Keywords:** Rheumatoid arthritis; Mucoadhesive buccal patch; Diclofenac diethylamine; Curcumin; sustain drug release;

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## 1. INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune condition that can be really debilitating. It affects about 1% of the global population, and it's known for ongoing synovial inflammation, a gradual breakdown of articular cartilage, plus eventual bone destruction. The whole pathogenesis of RA is basically tied to different immune cells moving in and out of the synovial membrane, especially activated T lymphocytes, B lymphocytes, macrophages, and neutrophils, which then drive the continuous release of pro-inflammatory cytokines, most notably tumour necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β) and interleukin-6 (IL-6). At the same time, there is increased oxidative stress coming from reactive oxygen species (ROS) inside that synovial space, so everything kind of snowballs, and it doesn't really stop. [1,2]. These interacting pathways keep the chronic inflammatory milieu going, which is responsible for pannus formation, osteoclast activation, and the irreversible joint damage that follows or something [3].

Current pharmacological management of RA encompasses non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, conventional synthetic disease-modifying antirheumatic drugs (csDMARDs; methotrexate, sulfasalazine, leflunomide), biologic DMARDs (anti-TNF agents, tocilizumab, rituximab), and Janus kinase (JAK) inhibitors (tofacitinib, baricitinib, upadacitinib)

[4,5]. Even with therapeutic progress, long-term oral medication delivery for RA is still kind of stuck with major limitations, like an extensive hepatic first-pass metabolism that gets in the way, plus gastrointestinal toxicity—ulceration, bleeding and hepatotoxicity- it's all there. There are also poor site-specific targeting, high dosing frequency, and systemic adverse effects that just keep stacking up over years of treatment[6,7]. These constraints have also stirred interest in alternative non-invasive routes for delivery that can keep therapeutic drug concentrations sustained at the target site while at the same time reduce systemic exposure more or less noticeably.

The buccal mucosa, if we think about it anatomically, is kind of a very convenient spot for transmucosal drug delivery. Its non-keratinised buccal epithelium is quite richly vascularised, and also relatively permeable so that drugs absorbed across it can enter systemic circulation quite directly. In other words, it helps you dodge both hepatic first-pass metabolism and gastrointestinal enzymatic degradation, which is sort of the point[8]. Mucoadhesive buccal patches use that anatomy somehow, by sticking to the mucosal surface, and so they prolong the drug-to-mucosa contact time, allowing a longer, steady drug release under conditions that are physiologically compatible, like ok basically, in the body[9]. Crucially, buccal patches can be removed immediately in the event of an adverse reaction, conferring an additional safety advantage not available with other routes.

Diclofenac diethylamine (DDEA) is an arylacetic acid-class NSAID that inhibits cyclooxygenase-1 and -2 (COX-1/COX-2), thereby reducing prostaglandin synthesis, pain, and inflammation. As a salt form of diclofenac, DDEA demonstrates enhanced aqueous solubility, superior membrane permeability, and topical/transdermal delivery efficacy relative to diclofenac sodium [10,11]. DDEA has an established pharmacokinetic profile (λmax 276 nm; molecular weight 369.29 g/mol; pKa ~4.0; half-life ~1–2 h) that makes it a suitable candidate for incorporation into controlled-release buccal systems intended to overcome its short elimination half-life [10].

Curcumin — (1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione — is a polyphenolic compound derived from the rhizome of Curcuma longa (turmeric) that exerts pleiotropic anti-inflammatory and antioxidant actions. Mechanistically, curcumin inhibits NF-κB activation, suppresses TNF-α, IL-1β, IL-6, COX-2, and inducible nitric oxide synthase (iNOS) expression, modulates MAPK/JAK-STAT and NLRP3 inflammasome signalling, and scavenges ROS — pathways central to RA pathophysiology [12,13]. Despite this broad anti-inflammatory profile and an excellent clinical safety record, curcumin is a BCS Class IV drug characterised by extremely poor aqueous solubility (~0.00021 mg/mL in distilled water), rapid presystemic metabolism, and low oral bioavailability, limiting systemic therapeutic application [14]. Formulation within a mucoadhesive polymer matrix addresses these limitations by providing a hydrophilic microenvironment that enhances dissolution and sustains mucosal delivery.

The rational combination of DDEA and curcumin in a single buccal patch is scientifically compelling: DDEA provides rapid COX-mediated anti-inflammatory analgesia while curcumin contributes multi-target immune modulation and antioxidant support, allowing potential dose reduction for each drug and, consequently, reduced individual drug-related side effects. Polymer-based mucoadhesive matrices employing HPMC (film former/controlled release) and PVP K30 (solubility enhancer/pore former) with Eudragit L100 as a unidirectional backing layer offer established clinical utility for such combination buccal delivery systems [15,16]. The present study therefore aimed to design, formulate, and systematically characterise six HPMC/PVP K30-based mucoadhesive buccal patch formulations (P1–P6) containing DDEA and curcumin, evaluate their physico-mechanical properties and in vitro drug release performance, and elucidate the drug release mechanism through kinetic modelling.

## 2. MATERIALS AND METHODS

### 2.1. Materials

HPMC 5 cps was taken from Qualikems Fine Chem Pvt. Ltd. (Vadodara, India); PVP K30 was bought from Molychem (Mumbai, India); PEG 400 from Sisco Research Laboratories Pvt. Ltd. (Maharashtra, India); glycerol from Avantor Performance Materials India Pvt. Ltd. (Thane, India); Eudragit L100 from Central Drug House Pvt. Ltd. (Delhi, India); curcumin from SharretsNutritions LLP (Jaipur, India) and diclofenac diethylamine from Suheka Industries (Ahmedabad, India). Every solvent and reagent used was analytical grade, in other words.

### 2.2. Preformulation Studies

#### 2.2.1. Organoleptic characterisation

The visual look, colour, smell, and flavour of the pure DDEA plus curcumin were checked by trained observers following the Indian Pharmacopoeia 2022 directions.

#### 2.2.2. Melting point determination

Melting points were established in triplicate using the capillary tube method on a digital melting point device (Remi, India), and reported as the mean ± SD.

**2.2.3. Solubility studies**

The equilibrium solubility for DDEA and curcumin was checked in distilled water, methanol and phosphate buffer pH 6.8. This was done by putting an excess amount of drug, about 50 mg, into sealed glass vials that already contained 10 mL of each solvent. After that, the vials were kept shaking continuously for roughly 24 h at 25 ± 1 °C. Then, the samples were filtered through 0.45 µm membrane filters and measured using UV–Vis spectrophotometry at the corresponding λmax values, with n = 3[17].

**2.2.4. UV spectrophotometry and calibration curves**

Standard stock solutions were prepared in methanol and serially diluted with phosphate buffer, pH 6.8, to construct calibration curves. Absorbance was measured at λmax 276 nm (DDEA) and 425 nm (curcumin) using a Shimadzu UV spectrophotometer (Kyoto, Japan). Linearity was established over 5–20 µg/mL (DDEA) and 2–10 µg/mL (curcumin)[19].

**2.2.5. Differential Scanning Calorimetry (DSC)**

DSC analyses (DSC 60, Shimadzu) were done on accurately weighed samples, sealed in aluminium pans, with a nitrogen purge. They were heated at 10 °C/min from 30 to 300 °C, and an empty sealed aluminium pan was used as the reference. The thermograms were collected for pure DDEA, pure curcumin, a physical blend, and the formulated patches to check drug–excipient compatibility and crystallinity[20].

**2.2.6. Fourier-Transform Infrared Spectroscopy (FTIR)**

FTIR spectra were acquired on a PerkinElmer spectrometer (ES version 10.6.2) across the wavenumber span 4000–651 $cm^{-1}$, where the spectra from pure DDEA, pure curcumin, the drug–drug physical mixture, and the drug–polymer system (HPMC + PVP K30) were laid side by side. The whole idea was to look for any possible incompatibilities between those components even if they're subtle or quietly hidden in the bands [20,22].

**2.3. Formulation of Mucoadhesive Buccal Patches**

The solvent-casting technique prepared six formulations (P1–P6). Accurately weighed quantities of HPMC and PVP K30 (as per Table 1) were dissolved in a water–ethanol co-solvent system under continuous magnetic stirring at 40 °C until a homogeneous, clear solution was obtained. Curcumin was pre-dispersed in ethanol and incorporated into the polymer solution under continuous stirring, followed by the addition of DDEA. PEG 400 and glycerol (combined plasticiser, as per Table 1) were added and mixed thoroughly. The resulting solution was degassed under vacuum for 15 min, poured onto levelled Teflon casting plates, spread to a uniform thickness with a calibrated applicator, and dried at 40 ± 2 °C in a hot-air oven for 24 h. The dried films were carefully peeled, conditioned for 24 h at ambient humidity, and laminated with an Eudragit L100 backing membrane to ensure unidirectional drug release. 2 × 2 cm patches were cut using a sharp steel die [18,21].

**Table 1. Composition of mucoadhesive buccal patch formulations P1–P6.**

| Ingredient (mg) | P1 | P2 | P3 | P4 | P5 | P6 |
|---|---|---|---|---|---|---|
| HPMC 5cps | 900 | 850 | 700 | 750 | 800 | 650 |
| PVP K30 | 300 | 350 | 500 | 450 | 400 | 550 |
| DDEA | 70 | 70 | 70 | 70 | 70 | 70 |
| Curcumin | 10 | 10 | 10 | 10 | 10 | 10 |
| Plasticiser (PEG 400 + Glycerol) | 20 % | 25 % | 35 % | 30 % | 25 % | 35 % |
| Solvent | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. |

**2.4. Evaluation of Physico-Mechanical Properties**

**2.4.1. Mass uniformity and weight variation**

Ten randomly selected patches per batch were individually weighed on an analytical balance (Citizen, India). Mean weight and percentage deviation from the mean were calculated. Three patches per formulation were also measured for thickness at three points using a digital micrometre screw gauge; results are expressed as mean ± SD [8].

**2.4.2. Surface pH**

A swollen patch (immersed in 1 mL distilled water for 2 h at room temperature) was brought into contact with a calibrated combination glass electrode, and pH was allowed to equilibrate for 1 min before recording [23].

**2.4.3.Folding endurance**

A 2 × 2 cm patch was folded repeatedly at the same point until fracture occurred. The number of folds before fracture represented the folding endurance value (n = 3)[24].

**2.4.4.Swelling index**

A 10 × 10 $mm^2$ film, on a pre-weighed coverslip, was put in a Petri dish with 50 mL phosphate buffer, pH 6.8. The film was then immersed there for the next step. The swollen film was removed,

blotted gently, and reweighed at 15-min intervals up to 120 min. Swelling index (%) = [(Xt − X₀)/X₀] × 100, where X₀ and Xt are initial and time-point weights, respectively[25].

#### *2.4.5.* Drug content uniformity

Three 20-mm disc pieces per formulation were put to dissolve in 100 mL phosphate buffer, pH 6.8, while stirring for 24 h, evenly, before moving on.After filtration, drug concentrations were determined by UV–Vis spectrophotometry at λmax 276 nm (DDEA) and 425 nm (curcumin). Drug content (%) was expressed as mean ± SD (n = 3)[8,9].

### 2.5. *In Vitro* Drug Release Study

*In vitro* drug release was kind of performed with a Franz diffusion cell (effective diffusion area 1.76 cm² ) kept at 37 ± 0.5 °C, and a 0.45 µm cellulose nitrate membrane was used as the synthetic barrier. The donor side held the patch (16 × 25 mm, active side facing toward the membrane) while the receptor side contained 15 mL of phosphate buffer pH 6.8, stirred at 50 rpm. Aliquots, 1 mL each were withdrawn at 0, 1, 2, 3, 4, 5, 6, 7 and 8 h and then swapped with the same volume of fresh buffer. After that the samples were measured by UV–Vis spectrophotometry at the respective λmax values, and cumulative drug release (%) was computed based on calibration curves[14,26].

### 2.6. Drug Release Kinetics

Release data from optimised formulation P6 were sort of fitted to zero order ($Q = K_0 \cdot t$), first order [$\ln(100 - Q) = -K_1 \cdot t$], Higuchi type matrix ($Q = KH \cdot t^{0.5}$) and Korsmeyer–Peppas ($\ln(Q/Q\infty) = n \cdot \ln(t) + \ln(K)$) models. The coefficient of determination, like $R^2$, was used to pick the best fit model, basically. For the Korsmeyer–Peppas exponent n, $n \leq 0.5$ means Fickian diffusion; $0.5 < n \leq 1.0$ shows anomalous non-Fickian transport, and $n > 1.0$ indicates super case-II transport [27].

## 3. RESULTS& DISCUSSION

### 3.1. Preformulation Studies

#### 3.1.1. Organoleptic properties and melting point

DDEA showed up as a white to off-white, odourless, a bit bitter crystalline powder, which matches the official monograph specifications pretty well. Curcumin, on the other hand, showed as a bright yellow-orange, fine crystalline powder, and it had a characteristic aromatic odour and a slightly bitter taste. When we did the melting point determination (Table 2), we got 156 ± 1 °C for DDEA and 180 ± 1 °C for curcumin, so it basically confirmed both the identity and the purity of each substance.

**Table 2: Melting point data for DDEA and curcumin (mean ± SD, n = 3)**

| Compound | Reading 1 (°C) | Reading 2 (°C) | Mean ± SD (°C) |
|---|---|---|---|
| Diclofenac diethylamine | 155–156 | 156–158 | 156 ± 1 |
| Curcumin | 179–180 | 180–182 | 180 ± 1 |

#### 3.1.2. Solubility studies

Solubility data (Table 3) showed that DDEA had a moderate aqueous solubility in distilled water (1.12 ± 0.06 mg/mL) and phosphate buffer pH 6.8 (2.04 ± 0.08 mg/mL), plus it was freely soluble in methanol (31.8 ± 1.4 mg/mL). Meanwhile, curcumin was basically not dissolving in water-type media (~0.00021 mg/mL in distilled water, ~0.00079 mg/mL in phosphate buffer pH 6.8) but it did dissolve well in methanol (52.6 ± 2.4 mg/mL), so it comes off as a BCS Class IV drug. That whole solubility gap kind of supports why PVP K30 was picked as a solubility-enhancing matrix component, and also why a hydroalcoholic casting solvent system was used to get a more even drug dispersion inside the polymer matrix.

**Table 3: Equilibrium solubility of DDEA and curcumin in selected solvents (mean ± SD, n = 3)**

| Solvent | DDEA (mg/mL) | Curcumin (mg/mL) |
|---|---|---|
| Distilled water | 1.12 ± 0.06 | 0.00021 ± 0.000 |
| Methanol | 31.8 ± 1.4 | 52.6 ± 2.4 |
| Phosphate buffer pH 6.8 | 2.04 ± 0.08 | 0.00079 ± 0.000 |

#### 3.1.3. UV spectrophotometry and calibration curves

Diclofenac diethylamine (DDEA) and curcumin exhibited maximum absorbance (λmax) at 276 nm and 425 nm, respectively, consistent with reported literature values and confirming their suitability for subsequent spectrophotometric analysis.

**Table 4:Photometric data of DDEA and curcumin**

| Sr. No. | DDEA Concentration (µg/mL) | DDEA Absorbance | Curcumin Concentration (µg/mL) | Curcumin Absorbance | DDEA Regression Equation ($R^2$) | Curcumin Regression Equation ($R^2$) |
|---|---|---|---|---|---|---|
| 1. | 5 | 0.13 | 2 | 0.25 | | |
| 2. | 10 | 0.29 | 4 | 0.57 | y = 0.0244x + | y = 0.1165x + |
| 3. | 15 | 0.37 | 6 | 0.73 | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| 4. | 20 | 0.51 | 8 | 1.04 | 0.020 (0.9857) | 0.055 (0.9840) |
| 5. | _ | | 10 | 1.18 | | |

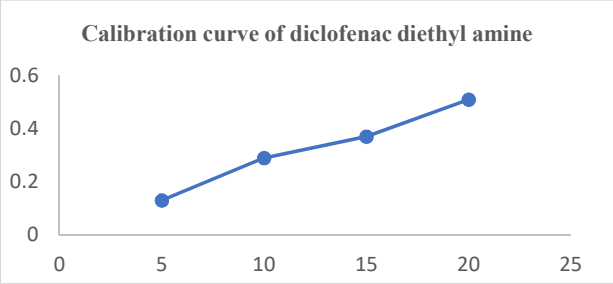



**Figure No. 1: Calibration curve of DDEA**

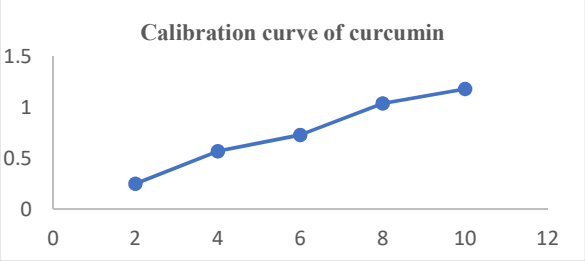
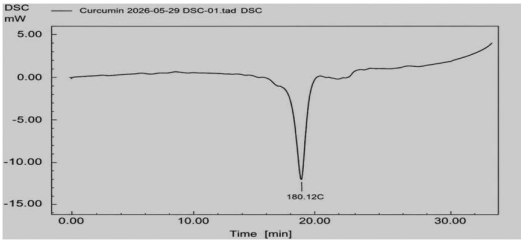



**Figure No. 2: Calibration curve of Curcumin**




**3.1.4.DSC analysis**

The DSC thermograms of DDEA and curcumin exhibited characteristic endothermic melting peaks at 156.45 °C and approximately 180 °C, respectively, confirming their crystalline nature. The retention of these peaks in the physical mixture and the formulated patch, without significant changes, indicated good physicochemical compatibility between DDEA and curcumin.

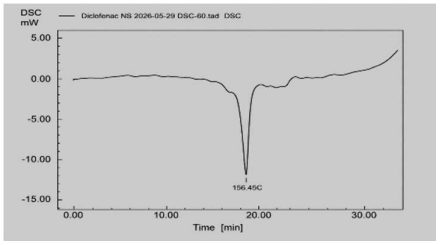
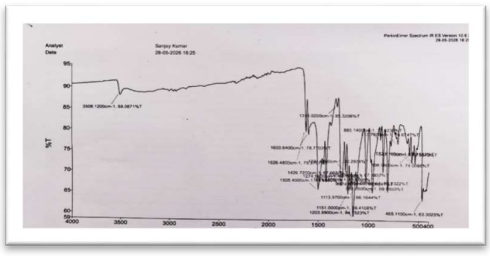


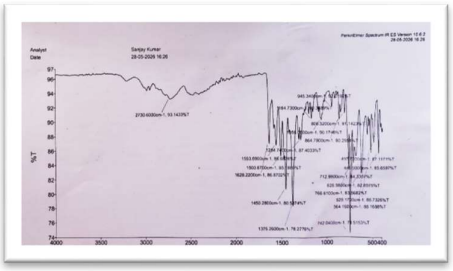

**Figure No. 3: DSC of DDEA**

**Figure No. 4: DSC of curcumin**

**3.1.5. FTIR analysis**



The FTIR spectra for DDEA and curcumin showed their own familiar functional group peaks at the expected wavenumbers, so everything looks pretty much right. In the physical mixture, and also in the formulated patch, the biggest peaks of both drugs stayed there, no real significant shifts and no disappearing acts. This kind of pattern suggests there was no real chemical interaction going on, and it also supports the idea that thedrugs are



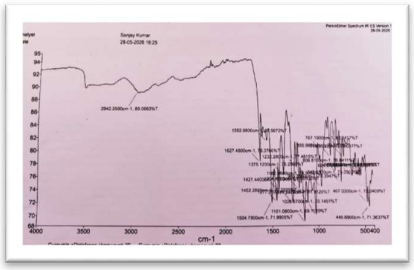
compatible with each other.

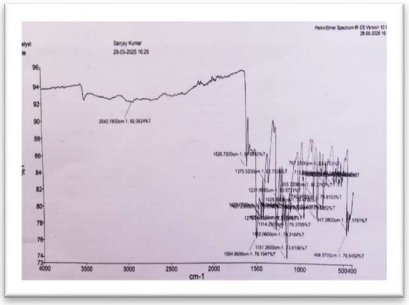
**Figure No. 5: FTIR of DDEA**

**Figure No. 6: FTIR OF Curcumin**

**Figure No. 7: FTIR of DDEA+Curcumin**

**Figure No. 8: FTIR of drug + excipients**





### 3.2. Physico-Mechanical Evaluation of Buccal Patches

#### 3.2.1. Mass uniformity, weight variation, and thickness

The outcomes shown in Table 5 which demonstrate that all formulations showed a fairly satisfactory level of weight and thickness uniformity. The patch weights were in the range of 250 to 256 mg, with a mean weight of around 252.7 ± 2.2 mg, which suggests minimal batch-to-batch variation and that the formulation components were distributed in a consistent manner. Also, the thickness of the patches stayed stable at 0.22 ± 0.01 mm across all the formulations, which confirms that the solvent-casting process is reproducible and, at the same time, it helps ensure uniformity of the prepared buccal patches.

#### 3.2.2. Surface pH

The surface pH of all formulations ranged from 6.72 to 6.84, and it is quite close to the physiological pH of the buccal mucosa. This near-neutral pH means there is good mucosal compatibility, and it also suggests the patches are not likely to annoy the area once they are placed, which can be seen in Table 5.

#### 3.2.3. Folding endurance

The folding endurance of all formulations ranged from 168 to 173 folds (mean 171.0 ± 1.8), which suggests excellent flexibility plus mechanical strength. The high values of folding endurance imply that the patches can handle day-to-day handling and buccal movements without any cracking or breakages, as shown in Table 5.

**Table 5: Mass uniformity, thickness, surface pH, and folding endurance data for formulations P1–P6.**

| Batch | Weight (mg) | % Deviation | Thickness (mm) | Surface pH | Folding Endurance (folds) |
|---|---|---|---|---|---|
| P1 | 250 | -1.06 | 0.21 | 6.72 | 172 |
| P2 | 253 | +0.13 | 0.22 | 6.80 | 170 |
| P3 | 256 | +1.32 | 0.22 | 6.76 | 168 |
| P4 | 252 | -0.26 | 0.23 | 6.84 | 173 |
| P5 | 254 | +0.53 | 0.21 | 6.79 | 171 |
| P6 | 251 | -0.66 | 0.22 | 6.75 | 172 |
| **Mean ± SD** | **252.7 ± 2.2** | — | **0.22 ± 0.01** | **6.78 ± 0.04** | **171.0 ± 1.8** |

#### 3.2.4. Swelling index

The swelling index for all the formulations went up, progressively, throughout the full 120-min study period. In the same way, the ones with more PVP K30 showed higher swelling, which suggests better water uptake capacity. This sort of more controlled swelling behaviour supports effective mucoadhesion and a sustained drug release profile while keeping the patch integrity stable, as can be seen in Table 6.

**Table 6: Swelling index (%) of buccal patch formulations P1–P6 in phosphate buffer pH 6.8**

| Time (min) | P1 | P2 | P3 | P4 | P5 | P6 |
|---|---|---|---|---|---|---|
| 15 | 29.8 | 31.2 | 30.5 | 31.5 | 30.2 | 30.9 |
| 30 | 52.4 | 55.2 | 53.8 | 54.6 | 53.1 | 55.8 |
| 45 | 73.2 | 76.7 | 75.0 | 75.8 | 74.1 | 77.5 |
| 60 | 94.5 | 99.5 | 97.0 | 98.2 | 95.8 | 100.8 |
| 90 | 115.6 | 122.0 | 118.8 | 120.4 | 117.2 | 123.5 |
| 120 | 132.4 | 138.6 | 135.8 | 137.2 | 134.0 | 140.1 |

#### 3.2.5. Drug content uniformity

The drug content of DDEA and curcumin across all formulations was within acceptable limits, ranging from 91.80–99.80% and 82.50–99.0%, respectively, as well. These results suggest a consistent distribution of the drug and solid, repeatable performance of the formulation process, sort of like a steady outcome, as shown in Table 7.

**Table 7: Drug content uniformity (%) of DDEA and curcumin in formulations P1–P6.**

| Batch | DDEA content (%) | Curcumin content (%) |
|---|---|---|
| P1 | 91.80 | 82.50 |
| P2 | 94.60 | 87.20 |
| P3 | 99.10 | 97.00 |
| P4 | 98.10 | 94.50 |
| P5 | 96.80 | 91.20 |
| P6 | 99.80 | 99.00 |
| **Mean ± SD** | 96.65± 3.12 | 91.90±6.23 |

### 3.3. *InVitro* Drug Release

The cumulative in vitro release of DDEA and curcumin went up steadily over 8 h for all formulations, as if it never really paused. DDEA release was about 91.5–99.8%, whereas curcumin release fell in the range of 82.5–99.0%, and formulation P6 ended up showing the greatest release of both agents, so it was picked as the optimized formulation. The stronger release seen with P6 might be tied to its higher PVP K30, plus more plasticizer included, while the relatively weaker curcumin release could be because curcumin has poor aqueous solubility, as displayed in Tables 8 and 9.

**Table 8: Cumulative *in vitro* drug release (%) of DDEA from formulations P1–P6.**

| Time (h) | P1 | P2 | P3 | P4 | P5 | P6 |
|---|---|---|---|---|---|---|
| 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 1 | 17.2 | 18.4 | 20.6 | 19.8 | 19.1 | 21.5 |
| 2 | 31.8 | 33.9 | 38.6 | 36.9 | 35.4 | 40.2 |
| 3 | 44.3 | 47.2 | 53.8 | 51.6 | 49.8 | 56.4 |
| 4 | 56.8 | 60.2 | 67.5 | 65.1 | 62.8 | 70.6 |
| 5 | 67.8 | 71.4 | 79.6 | 76.9 | 74.3 | 82.1 |
| 6 | 76.5 | 80.4 | 87.9 | 85.2 | 82.8 | 90.1 |
| 7 | 82.6 | 86.9 | 92.5 | 90.6 | 88.7 | 93.8 |
| 8 | 88.4 | 91.2 | 94.1 | 93.0 | 92.0 | 95.6 |

**Table 9: Cumulative in vitro drug release (%) of curcumin from formulations P1–P6**

| Time (h) | P1 | P2 | P3 | P4 | P5 | P6 |
|---|---|---|---|---|---|---|
| 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 1 | 8.4 | 9.1 | 10.8 | 10.2 | 9.6 | 11.5 |
| 2 | 16.7 | 18.4 | 22.3 | 21.0 | 19.8 | 24.5 |
| 3 | 26.5 | 29.0 | 34.8 | 33.0 | 31.2 | 37.8 |
| 4 | 37.2 | 40.4 | 47.9 | 45.8 | 43.5 | 52.1 |
| 5 | 47.8 | 52.1 | 60.8 | 58.6 | 56.0 | 65.8 |
| 6 | 58.5 | 63.2 | 73.5 | 69.9 | 67.1 | 77.9 |
| 7 | 67.9 | 73.1 | 82.4 | 80.0 | 77.6 | 85.8 |
| 8 | 75.8 | 81.2 | 88.5 | 86.9 | 84.8 | 90.7 |

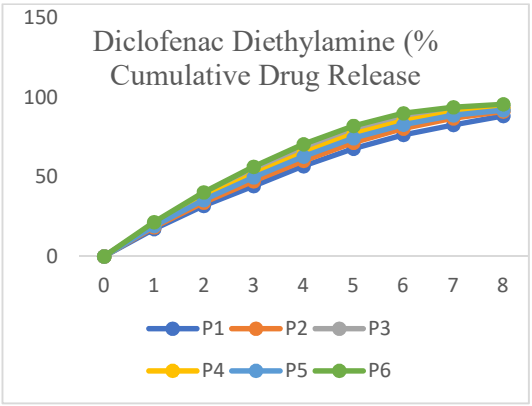



**Figure No. 9: In vitro drug release of DDEA**

**Figure No.10: In vitro drug release of Curcumin**

### 3.4. Drug Release Kinetics of Optimized Formulation P6

The release kinetics of the optimized formulation (P6) are presented in Table 10. The Higuchi matrix model showed the best fit for both DDEA ($R^2$ = 0.9909) and curcumin ($R^2$ = 0.9785), indicating Fickian drug release. The results suggest that drug release occurred through diffusion, providing controlled and sustained release from the buccal patch.

**Table 10: Kinetic model parameters for DDEA and curcumin release from optimised formulation P6.**

| Kinetic Model | Parameter | DDEA Value | Curcumin Value | $R^2$ (C / D) |
|---|---|---|---|---|
| Zero order | $K_0$ (% $h^{-1}$) | 10.7060 | 11.8840 | 0.9842 / 0.9382 |
| First order | $K_1$ ($h^{-1}$) | 0.4339 | 0.3282 | 0.9113 / 0.9525 |
| Higuchi matrix | KH (% $h^{-0.5}$) | 42.8462 | 46.3224 | 0.9909 / 0.9785 |
| Korsmeyer–Peppas | n (exponent) | 0.7347 | 1.0204 | 0.9785 / 0.9484 |

#### 3.4.1Zero-Order Kinetics

The zero-order kinetic model showed $R^2$ values of 0.9842 for curcumin and 0.9382 for DDEA,

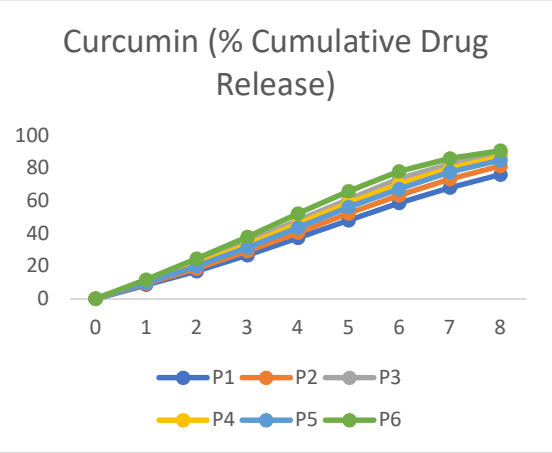
indicating that drug release from formulation P6 did not strictly follow concentration-independent release, as presented in Figures11 and 12.

**Figure no.11: zero-order graph of DDEA**

**Figure no.12: zero-order graph of curcumin**

**3.4.2 First Order Kinetics**

The first-order kinetic model showed moderate fitting for curcumin ($R^2$ = 0.9113) and DDEA ($R^2$ = 0.9525), suggesting that drug release from formulation P6 was only partially dependent on the remaining drug concentration, as shown in Figures 13 and 14.



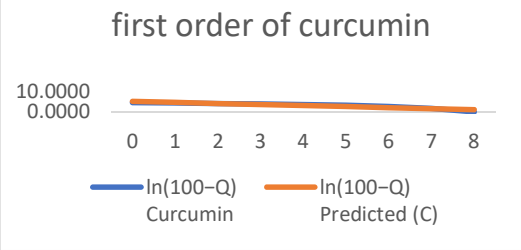
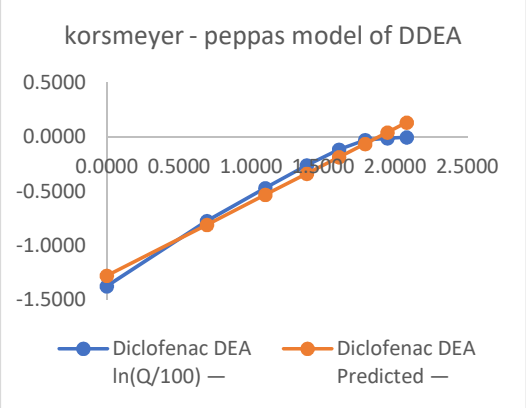




**Figure No. 13: First-order graph of DDEA Figure No. 14: First-order graph of curcumin**

**3.4.3 Higuchi matrix model**

The Higuchi model exhibited high correlation coefficients for curcumin ($R^2$ = 0.9909) and DDEA ($R^2$ = 0.9785), indicating that diffusion through the hydrated polymer matrix was a major mechanism governing drug release from formulation P6, as shown in Figures15 and 16.



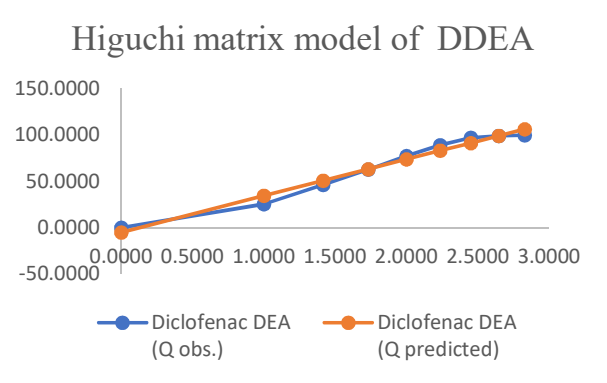




**Figure No.15: Higuchi matrix of DDEA**

**Figure No. 16: Higuchi matrix of curcumin**

**3.4.4 Korsmeyer-Peppas model**

The Korsmeyer–Peppas model provided the best fit for both curcumin ($R^2$ = 0.9785, n = 1.0204) and diclofenac diethylamine (DDEA) ($R^2$ = 0.9484, n = 0.7347). The release exponent (n) values indicate anomalous (non-Fickian) transport, suggesting that drug release occurs through a combined mechanism of diffusion and polymer swelling or relaxation. These findings are illustrated in Figures 17 and 18.

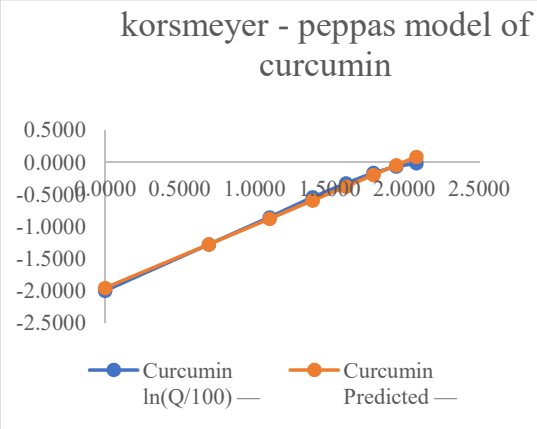



**Figure No. 17: Korsmeyer-Peppas of DDEA curcumin**

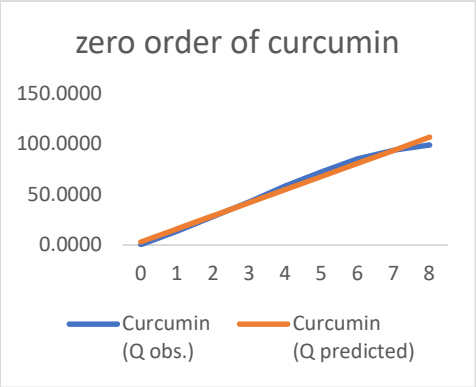



**Figure No. 18: Korsmeyer-Peppas of**

## 4. CONCLUSION

The present study successfully developed and characterized mucoadhesive buccal patches that incorporated diclofenac diethylamine along with curcumin in order to support sustained management of rheumatoid arthritis. The formulations that were prepared showed good physicochemical and mechanical features, such as fairly uniform weight and thickness, close to neutral surface pH, adequate folding endurance, controlled swelling behaviour, and consistent drug content, and this, in turn, suggests the solvent-casting method is reproducible. Out of the six formulations, P6 looked the most attractive in overall terms, because it gave the highest cumulative drug release in 8 h, reaching 95.6% for diclofenac diethylamine and 90.7% for curcumin. FTIR and DSC results also backed up that the drugs and the chosen polymers are compatible, showing no major physicochemical interactions, or at least none that were statistically meaningful. Then, the drug release kinetic assessment pointed toward the Higuchi diffusion model plus the Korsmeyer–Peppas model, meaning the release is likely happening via both diffusion and polymer swelling, which they described as non-Fickian transport. In general, this buccal patch seems like a promising sustain-release approach that could enhance therapeutic efficacy, lower dosing frequency, and reduce gastrointestinal side issues linked with traditional oral therapy. That said, more ex vivo permeation, in vivo pharmacokinetic and pharmacodynamic work, plus long-term stability studies are still needed before we can really say it has clinical applicability and solid therapeutic potential.

## DECLARATION OF INTERESTS

The authors declare no competing financial interests or personal relationships that could have influenced the work reported in this paper.

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