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# STUDIES ON FORMULATION AND EVALUATION OF BILAYERED TABLETS

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## ABSTRACT

Bilayer tablet represents a new era in the successful development of controlled release formulations, as well as a number of other features that contribute to the development of a successful drug delivery system. In order to minimise chemical incompatibilities across APIs through physical separation and to allow for the development of diverse drug release profiles, bilayer tablets can be an excellent first choice.

The bi-layered pill represents a completely different approach to anti-inflammatory and analgesic medication. One of the goals of this study was to design and analyse bilayered curcumin tablets for their efficacy in the treatment of inflammation.

It was possible to construct the immediate-release layer by utilising super dis-integrants such as SSG and a binder such as xantham gum, while the sustained-release layer was achieved by using hydrophilic polymers such as HPMC K 100 or PVP. All of the pre-formulation parameters were checked prior to the preparation of the tablets, and the curcumin tablets were prepared using the direct compression method and evaluated for physical characteristics such as hardness, weight variation, drug content, and friability before being used in the study.

To determine the in-vitro release of the medication, the researchers used a USP type I dissolution test device using dissolution media of 0.1N HCl and phosphate buffer pH 7.4 as dissolution media, with dissolution continuing for 12 hours to determine the sustained release layer. It was discovered that all of the formulations were within the acceptable range of the standard. Drug release from the tablet ranged between 82.44 percent and 88.20 percent in the first 12 hours after swallowing the tablet.

The Higuchi model and first-order kinetics are used to predict the rate of drug release. It was determined that the F4 formulation produced the best results when used as a bilayered tablet for the effective treatment of inflammation in the test subjects.

Keywords: Bi-layered Tablet, Formulations, Drug Release.

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## 1. INTRODUCTION

Besides being suitable for the sequential release of two drugs in combination, the bilayer tablet is also capable of separating two different types of incompatible substances. It can also be used for sustained release tablets, in which one layer is immediate release as the initial dose and the second layer is the maintenance dose, among other things. A bilayer tablet is an excellent example of avoiding chemical incompatibilities between the active pharmaceutical ingredients (APIs) while still enabling distinct drug release characteristics (Immediate release with extended-release). In a bilayer tablet, the first layer serves a loading dosage purpose, while the second layer serves a maintenance dose purpose, with the first layer serving as the loading dose. Curcumin is a brilliant yellow substance generated by the Curcuma longa plant and it has anti-inflammatory properties. It is the primary curcuminoid found in turmeric (Curcuma longa), which is a member of the ginger family, Zingiberaceae, and is derived from the root of the turmeric plant. Herbal supplements, cosmetic ingredients, food flavouring, and food colouring are all excellent uses for this plant. Curcumin exerts its powerful anti-inflammatory and anti-carcinogenic effects via regulating a number of signalling molecules in various tissues. Several key elements in cell signal transduction pathways relevant to growth, differentiation, and malignant transformation have been shown to be suppressed by curcumin in vitro; it has been demonstrated in vivo that curcumin inhibits protein kinase, prostaglandin biosynthesis, and the expression of the enzyme $(COX)^{-2}$.

The majority of excretion occurs through faecal excretion, with a tiny percentage occurring through biliary excretion. In medicine, they are used as an anti-inflammatory, an antioxidant, to lessen the chance of developing brain illnesses, to prevent and cure Alzheimer's disease, rheumatoid arthritis, and depression, among other things. According to the literature, curcumin possesses anti-inflammatory characteristics and is therefore utilised in the treatment of rheumatism. However, curcumin has poor bioavailability due to its low aqueous solubility. The current work aims to develop bilayered curcumin tablets, in which one layer provides quick release as an initial dose and the second layer provides a maintenance dose, in order to improve its bioavailability for the efficient treatment of inflammation. In this study, an attempt was made to manufacture a bilayered tablet of curcumin by direct compression in order to maximise its bioavailability and, as a result, reduce the number of times it was taken.

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## 2. MATERIALS AND METHODS

**MATERIALS**

Curcumin, dicalcium phosphate, hydroxypropyl, methylcellulose, microcrystalline cellulose and xanthan gum were procured from Akums Drugs & Pharmaceuticals Limited, Haridwar. All the other chemicals and reagents used in this study were of analytical grade.

**METHODS**

**Drug-Excipient Interaction Study:**

In order to develop and formulate a good dosage form, it is necessary to take into account the physical, chemical, and biological features of both the drug and the excipients that are employed in its manufacturing. Compatibility between the active component and additional excipients must be established in order to develop a product that is stable, effective, visually appealing, and safe. As a result, the Fourier Transform Infrared Spectroscopy (FT-IR) technique was used to determine the compatibility of curcumin with the excipients used in the final formulation before it was manufactured.

**FT-IR Spectral Investigation:**

Pallets for the IR spectra were made by mixing samples of pure drug, IR layer composition, and SR layer composition with KBr, which were then scanned using a Shimadzu FTIR 8400 spectrophotometer to obtain the IR spectra.

**Bilayer Tablets are made in the following ways:**

In this work, an attempt was made to develop six curcumin formulations, with the content of the immediate-release layer remaining the same in all six formulations while the composition of the sustained-release layer changed.

**IMMEDIATE RELEASE LAYER**

**TABLE 1 COMPOSITION OF IMMEDIATE RELEASE LAYER**

| **Ingredients** | **Quantity** |
|---|---|
| Curcumin (mg) | 20mg |
| Xantham Gum | 10mg |
| Sodium Strach Glycolate | 12mg |
| Dicalcium Phosphate | 24mg |
| Microcrystalline Cellulose | 84mg |
| Colorant | QS |
| Total | 150 mg |

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**SUSTAINED RELEASE LAYER**

**TABLE 2 COMPOSITION OF SUSTAINED RELEASE LAYER**

| **Ingredients** | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|
| Curcumin | 30 mg | 30 mg | 30 mg | 30 mg | 30 mg | 30 mg |
| Poly vinyl Pyrrolidone | 0 | 0 | 10 mg | 20 mg | 10 mg | 15 mg |
| Hydroxy Propyl Methyl Cellulose | 10 mg | 20 mg | 0 | 0 | 10 mg | 5 mg |
| Xantham Gum | 20 mg | 20 mg | 20 mg | 20 mg | 20 mg | 20 mg |
| Micro Crystalline Cellulose | 132 mg | 132 mg | 132 mg | 132 mg | 132 mg | 132 mg |
| Total | 200 mg | 200 mg | 200 mg | 200 mg | 200 mg | 200 mg |

**Preparation**

Sodium starch glycolate and xantham gum were used to make the immediate-release layer, and hydrophilic polymers like HPMC K 100 and PVP were used to make the long-term release layer. Each ingredient is shown in a formulation table. Before making tablets, all pre-formulation parameters were checked and the drug and other ingredients were mixed together to make a premix that could be compressed into tablets right away.

**Content of Drug**

Sodium starch glycolate and xantham gum were used to make the immediate-release layer, and HPMC K 100 and PVP were used to make the sustained-release layer. Each ingredient is shown in a formulation table. Before making tablets, all pre-formulation parameters were checked and the drug and other ingredients were mixed to make a premix that could be compressed into tablets right away.

## 3. RESULTS AND DISCUSSION

**Drug and Excipient Interaction Study**

The FTIR studies were carried out as mentioned in the method. Major functional groups present in curcumin show characteristic peaks in IR spectrum.

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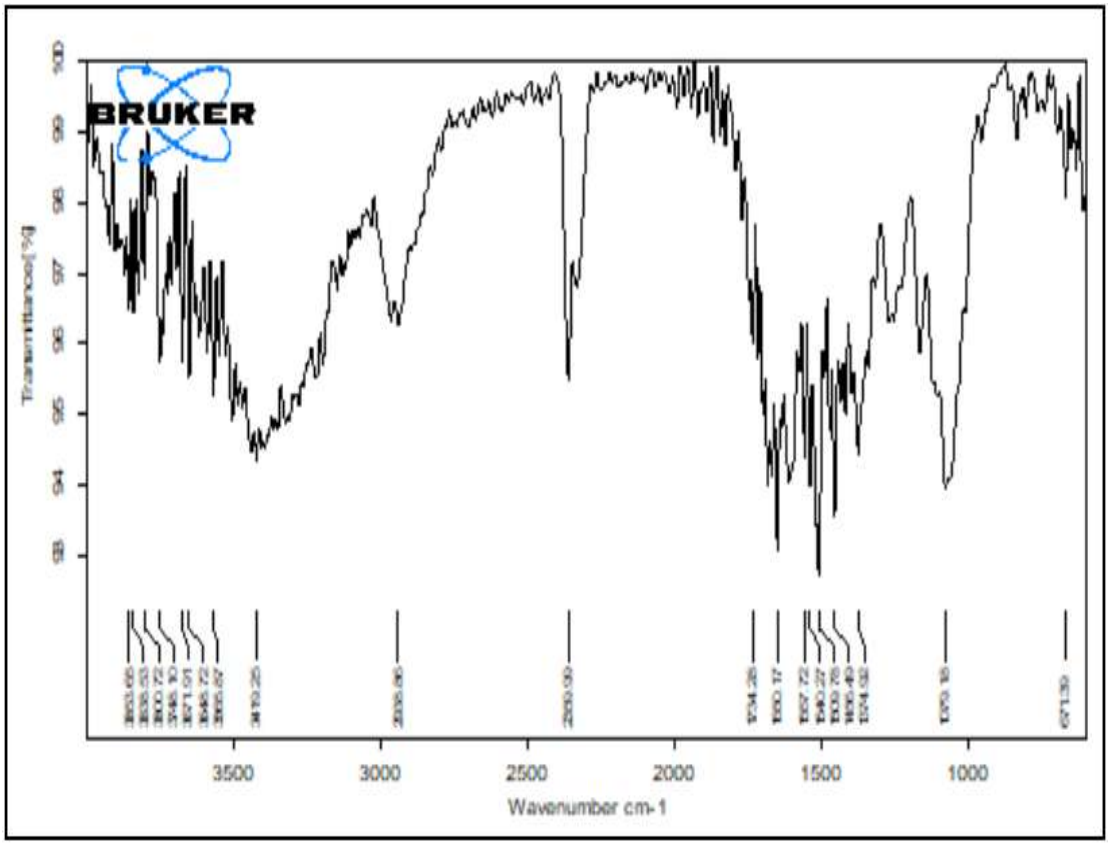


**FIG 1 FTIR SPECTRA OF CURCUMIN**

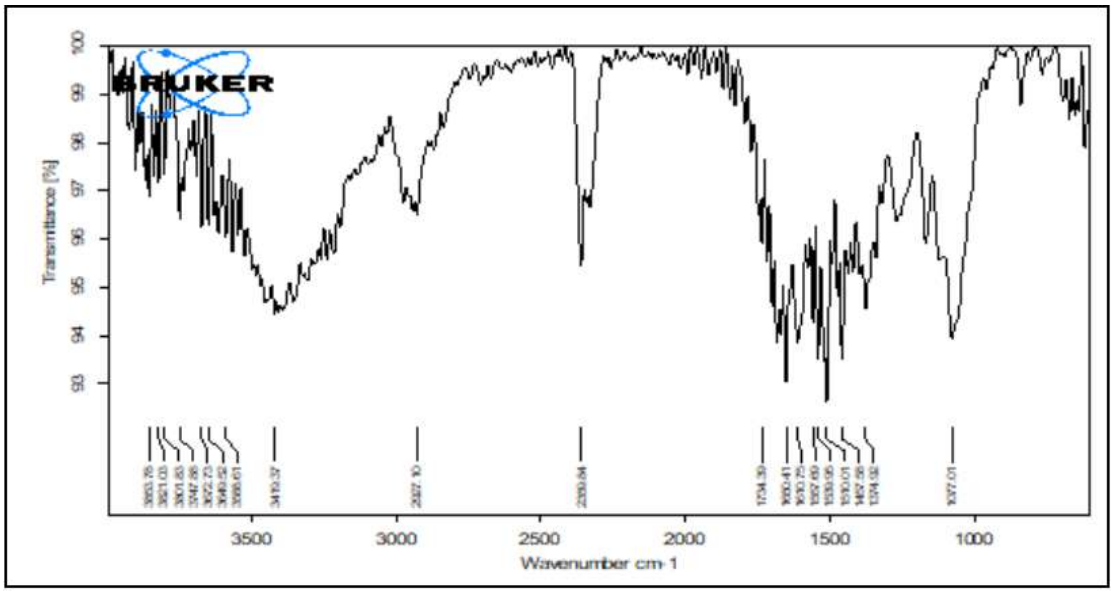


**FIG. 2: FTIR SPECTRA OF CURCUMIN+ EXCIPIENTS**

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Curcumin's infrared spectrum, shown in Fig. 1, has a characteristic absorption band that may be identified. The characteristic absorption bands for major functional groups of pure drugs and physical mixtures of drugs and excipients can be determined using Fourier transform infrared (FTIR) investigations. It was discovered that curcumin's distinctive bands are not affected and may be successfully manufactured without any change in their position, indicating that there are no chemical interactions between the medicine and the excipients, according to FTIR spectra.

**Immediate Release Layer:**

Pre-formulation study of the IR batches are shown in Table 3, where bulk density is 0.51 gm/ml, tapped density is found to be 0.64 gm/ml, Carr's index is 10.31, Hausner's ratio was 1.10, angle of repose is 31.79°. From these obtained results prepared blends were found to possess good flow properties and ready for compression into tablets.

**Table 3 Evaluation Layer of Immediate Release**

| Formulation | Bulk density ±SD | Tapped density* ±SD | Compressibility Index *±SD | Hausner's ratio*±SD | Angle of repose*±SD |
|---|---|---|---|---|---|
| IR Layer | 0.50±0.001 | 0.64±0.011 | 10.31±0.18 | 1.10±0.051 | 31.79±0.414 |

**Sustainable Release Layer**

Table 4 Evaluation Layer of Sustained Release

| Formulation | Bulk density ±SD | Tapped density* ±SD | Compressibility Index *±SD | Hausner's ratio*±SD | Angle of repose*±SD |
|---|---|---|---|---|---|
| F1 | 0.49±0.003 | 0.66±0. 011 | 12.41±0.20 | 1.10±0.01 | 38.39±0.456 |
| F2 | 0.47±0.005 | 0. 62±0.01 | 12.82±0.367 | 1. 09±0. 02 | 37.53±0.671 |
| F3 | 0.50±0.0051 | 0.62±0.017 | 12.92±0.290 | 1.12±0.030 | 38.70±0.579 |
| F4 | 0.51±0.0050 | 0. 67±0.015 | 13.20±0.235 | 1.11±0.072 | 36.97±0.715 |
| F5 | 0.50±0.01 | 0.65±0.01 | 13.13±0.215 | 1. 12±0.025 | 37.12±0.527 |
| F6 | 0.49±0.015 | 0. 63±0.025 | 12.78±0.325 | 1.10±0. 020 | 37.03±0.717 |

*Average of six determinations, SD-Standard deviation

Pre-formulation study of the SR batches are shown in Table 4, where bulk density in the range of 0.47-0.51 gm/ml, tapped density shown in the range of 0.62-0.67 gm/ml, Carr's index was 12.41-13.78, Hausner's ratio was 1.09-1.12, angle of repose is 36.97- 38.39º. The results of the prepared blends showed that they possess good flow properties and ready for compression into tablets.

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## 4. CONCLUSION

The current work comprises the formulation and assessment of bilayered curcumin tablets made from HPMC K 100 and PVP, which serves as a retardant polymer in the formulation. Drug-excipient compatibility investigations indicated that the drug is compatible with the polymers HPMC K 100 and PVP, which were chosen for testing. The pre-compression parameters and the post-compression parameters were acquired from both layers and were found to be within acceptable ranges in both cases. The direct compression method was used to create the tablets in this study. The post-compression parameters remained within the prescribed ranges, which was good news. Curcumin bilayered tablets with an optimised formulation design were successfully created and made, with all parameters being constantly monitored and assessed throughout the process. The amount of PVP and HPMC K100 used was determined to be the most important aspect to optimise. Because there was no significant change in the peak of curcumin observed during the analysis of the IR spectra, it was concluded that there was no interaction between the medicine and the other excipients used in the study. The results of the post-compression experiments were within the boundaries of pharmacopeial standards, as was expected. The tablets demonstrated an instantaneous release of the drug to provide the loading dose, followed by a sustained release of the drug for up to 12 hours. The in-vitro drug release from the tablets demonstrates a considerable improvement in drug dissolution compared to the previous study.

The formulation F4 demonstrated the highest release rate of 88.98 percent among the six formulations tested, and it can be called the best formulation overall. The First order and Higuchi models provided a better explanation for the kinetic release studies of the best formulation, which suggested that the release of medicines from the formulation occurs through a diffusion mechanism. According to the results of the stability studies, the formulation remained stable, and no significant differences were noted between the results of the stability studies and the results of the tests.

The optimization of bilayer tablet dosage form may therefore represent a viable formulation for the distribution of pharmaceuticals from a single dosage form, which could reduce the frequency of medication administration, improve patient compliance and result in improved disease management. From an industrial standpoint, there are no impediments to the large-scale production of bilayered tablet formulations. In addition, when compared to other controlled release dosage forms, the formulation is more cost-effective than the alternatives. As a result, this tablet will undoubtedly serve as a new point of emphasis for researchers who are interested in developing modified continuous release dosage forms in a cost-effective manner.

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