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Original article

Formulation and Evaluation of Clindamycin hydrochloride Dental Implants for the Treatment of Periodontitis

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ABSTRACT:
The purpose of the work was to formulate and evaluate Dental implant for delivery of Clindamycin hydrochloride locally into periodontal pocket. Dental implants were prepared by solvent casting method using polymers such as Chitosan, Hydroxyl propyl methyl cellulose K4M, Carboxyl methyl cellulose Na and Polyethylene glycol 400 as a plasticizer. The prepared Dental implants were evaluated for physicochemical parameters such as Weight uniformity, Thickness, Surface pH, Folding endurance, Tensile strength, Percentage moisture loss, Drug content uniformity and in-vitro antibacterial study. FT-IR and DSC study reveals that there is no interaction between the Clindamycin hydrochloride and polymers. From SEM studies it was observed that the prepared implants are having smooth surface. *In-vitro* drug release studies were carried out for Dental implants by static dissolution method. All the formulation were able to sustain drug release over a period of 24 hours. The drug release from the prepared Dental implants fitted Peppas Model and the mechanism follows non- Fickian drug release. Based on the results obtained from the physicochemical parameters and in-vitro drug release CDH 9 was found to be optimized formulation. In-vitro antibacterial study was carried out on *S.aureus* had an inhibitory effect incubation. The short term stability of optimized formulation revealed that the drug remained intact and stable in the Dental implants during storage. Hence, low dose, site-specific Clindamycin hydrochloride implants is a potential tool for the curing of periodontitis.

Keywords: Dental implants, Periodontitis, Local drug delivery, Clindamycin hydrochloride, Chitosan.

1. INTRODUCTION

Novel Drug Delivery is the new branch of Pharmaceutical which is considered as best eminent technique for Targeted Drug Delivery system [1]. Among many NDDS, Implantable drug delivery systems allow targeted and localised drug delivery and may achieve a therapeutic effect with lower concentrations of drug. As a result, this may minimise potential side-effects of therapy, while offering the opportunity for better patient compliance. This type of system also has the potential to deliver drugs which would normally be unsuitable orally because it avoids first pass metabolism and chemical degradation in the stomach and intestine, thus, increasing bioavailability [2].

An IDDS is defined as a system in which the implant is inserted into the body by surgery. IDDS seems to be a very stronger drug delivery system, medications that are less bioavailable by the digestive tract. Example of IDDS includes Antibiotics, including NSAIDS, is mostly contraceptives, etc [3]. Implantable drug delivery devices are particularly desirable where compliance with a prescribed drug regimen is critical. Such devices allow a drug to be delivered at a specific rate without regular physician or patient intervention [4]. Several implantable devices like fibers, films, Dental implant and gels were used [5].

A site-specific system called Dental implants aims at delivering the active constituent at sufficient levels inside the periodontal pockets and at the same time minimizing the side effects associated with systemic drug administration.6 Thus the Dental implant could be easily placed into periodontal pocket [6].

Periodontal disease is considered as a major public health problem throughout the world. Good daily oral hygiene which plays a vital role in maintaining healthy gums and teeth [7]. Periodontal disease is one of the world's most prevalent chronic oral diseases affecting more than 50% of Indian community and occurs in all groups, ethnicities, races, genders and socioeconomic levels [8]. The term Periodontitis comes from two terms "Peri' = around, "Odont" = tooth, "Itis" = inflammation [9]. Periodontal diseases are infections of the structures around the teeth, which include the gums, periodontal ligament and alveolar bone.

Periodontal diseases are of two types: gingivitis and periodontitis.

Gingivitis may lead to a more serious condition called periodontitis, in which the inner gum and bone pull away from teeth and form pocket. These pockets can collect bacteria and debris, and become infected or abscessed [10]. These pockets provide an ideal environment for the growth and proliferation of aerobic and anaerobic pathogenic bacteria [11] *Porphyromonas gingivalis, Prevotella intermedia, Fusobacterium nucleatum, Campylobacter rectus, Prevotella melaninogenica,* and *Actinobacillus actinomycetemcomitans* etiology of periodontal diseases has been well established [8]. One of the clinical features of the periodontal disease is the formation of periodontal pockets. Normally the gap between the gingival and the tooth is 1-3 mm deep but it usually exceeds 5mm to 10mm during diseased conditions [12].

Usually therapy of periodontics is based on scaling, surgery and the use of antibiotics (e.g. Tetracycline, Minocycline, Clindamycin, Metronidazole, Chlorhexidine, Ornidazole and Quinolones).Treatment to periodontitis with a localized drug delivery system aims at delivering therapeutic agent at a sufficient concentration inside the periodontal pocket and at the same time minimizes the side effects associated with systemic drug administration [11].

Clindamycin is a lincosamide with a broad spectrum, being active against aerobic, anaerobic, and β-lactamase producing bacteria [13]. Clindamycin is used primarily to treat anaerobic infections caused by susceptible anaerobic bacteria, including dental infections [14]. Clindamycin is highly active against streptococci, pneumococci and staphylococci. *Bacteroides fragilis*, *Clostridium* and other anaerobes are usually susceptible. Clindamycin is well absorbed orally. Food does not interfere with its absorption. It penetrates well in most tissues, including bones and phagocytes, except CSF [15] the t1/2 is 3 hours [16]. The usual adult dose by mouth is 150-300 mg every 6 hrs [15].

The aim of this study is to prepare Clindamycin hydrochloride (CDH) Dental implants loaded with suitable biocompatible and biodegradable polymers for periodontal applications and examines the effects of the concentration of polymers used and the volume of polymer solutions on the characteristics of the Dental implants. After thorough review of literature we found that there is no published data regarding stated drug and polymer combination as Dental implants for periodontal use, hence we have selected this study.

2. MATERIALS AND METHOD

Clindamycin hydrochloride was procured Aarthi Pharmaceuticals Ltd. Mumbai, India. Chitosan was purchased from HI media laboratories Pvt. Ltd, Hydroxyl propyl methyl cellulose K4M, Carboxy methyl cellulose sodium were purchased from Yarrow Chemicals Pvt. Ltd. All chemicals and solvents used are of high analytical grade.

2.1. Preparation Clindamycin hydrochloride dental implants:

Dental implants was prepared by solvent casting technique; an accurately weighed amount of Chitosan was soaked in 75ml of water containing 0.75ml of acetic acid for 24 hours to get a clear solution, which was filtered through muslin cloth to remove undissolved polymer (chitin). Then, the accurately weighed amounts of copolymers (HPMC K4M, CMC Sodium) in varying concentrations were added. Mixing was continued until a clear solution of polymers in solvent was obtained. After the complete dissolution of the polymer. A measured quantity Propylene glycol 400 (as a plasticizer) was added to the polymer solution. Accurately weighed amount of drug was added and vortexed for 15 minutes, to dissolve the drug in polymeric solution. This dispersion was kept aside for 30 minutes for expulsion of air bubbles. The solution was poured into a clean glass petriplate placed on a horizontal plane. Then it was allowed to dry at room temperature for 48 hours. After drying the implants were cut into strips of the required size (8x2 mm^2). These were wrapped in aluminium foil and stored in a desiccator until further use [9, 17].

2.2. Calculation of Clindamycin hydrochloride dose to be incorporated in the dental implants [9]

Clindamycin hydrochloride is available in the market as a capsule (300 mg). Thus oral therapy with 300 mg every 6 hours is substituted as soon as possible. The dose of sustained release implants is reduced to 1/400 that of the capsule form therefore a dose of 0.75 mg per Dental implants was fixed.

Internal diameter of petridish = 8.8 cm

Internal surface area of petridish = πr^2

= 22 / 7 x $(4.4)^2$

= 60.84 cm^2

= 6084 mm^2

Surface area of Dental implants= 0.8 x 0.2 cm^2

= 0.16 cm^2

= 16 mm^2

Therefore, 16 mm^2 contains 0.75 mg of Clindamycin hydrochloride

6084 mm^2 contains X mg of Clindamycin hydrochloride

X = 285.1 mg of Clindamycin hydrochloride

Formulation table of Clindamycin hydrochloride dental implants

Table 1: Formulation of Clindamycin hydrochloride Dental implants

Formulation code	Drug (mg)	Chitosan (mg)	HPMC K4M (mg)	CMC Na (mg)	PEG 400 (ml)	Water (ml)	Acetic acid (ml)
CDH 1	285	1000	-	-	0.5	75	0.75
CDH 2	285	1000	1000	-	0.5	75	0.75
CDH 3	285	1000	900	100	0.5	75	0.75
CDH 4	285	1000	800	200	0.5	75	0.75
CDH 5	285	1000	700	300	0.5	75	0.75

CDH 6	285	1000	600	400	0.5	75	0.75
CDH 7	285	1000	500	500	0.5	75	0.75
CDH 8	285	1000	400	600	0.5	75	0.75
CDH 9	285	1000	300	700	0.5	75	0.75
CDH 10	285	1000	200	800	0.5	75	0.75
CDH 11	285	1000	100	900	0.5	75	0.75
CDH 12	285	1000	-	1000	0.5	75	0.75

2.3. Drug – Polymers Compatibility Study

The compatibility of polymers and drug were evaluated by FT-IR and DSC.

2.3.1. FT-IR Study

FT-IR spectra of pure drug, polymers, physical mixture of drug-polymers and drug loaded implants were analyzed using FT-IR Spectrophotometer (BRUKER ALPHA E). The FT-IR spectra of combined polymers and drug were compared with standard pure drug. The samples were placed into sample holder and scanned in the spectral region between 4000 cm^{-1} and 600 cm^{-1}.

2.3.2. Differential scanning calorimetry

Thermal analysis of pure drug and physical mixture of drug-polymers was analyzed using DSC-60 calorimeter (Shimadzu, Japan). The Samples of pure drug and physical mixture of drug-polymers was taken in an aluminium pan sealed with aluminium cap and kept under nitrogen purging (atmosphere) with a flow rate of 50 ml/min. The samples were scanned from 0-300^{o}C with the heating rate of 10^{o}C rise/min using differential scanning calorimeter [18].

2.3.3. Scanning electron microscope

A scanning electron microscope (ZEISS EVO LS 15) was used to study the surface characteristics of the implants. Implants were sputter coated using an electrically conducting metal such as gold [19].

2.4. Evaluation of clindamycin hydrochloride dental implants

2.4.1. Weight Uniformity

The weight uniformity test was carried out by weighing 6 implants cut from different places of the same formulation of known size (8x2 mm^2) and their individual weights were determined by using the electronic balance. The mean value was calculated [20].

2.4.2. Thickness

The thickness of the implant was measured by screw gauge with least count of 0.01mm. An average of 6 values determined at 6 different points on the implants was calculated [21].

2.4.3. Surface pH

Dental implants were allowed to swell for 3 hour on the surface of the agar plate, prepared by dissolving 2% (w/v) agar in double distilled water under stirring and then pouring the solution into the petridish to solidify at room temperature. The surface pH was measured by means of pH paper placed on the surface of the swollen implants [22].

2.4.4. Folding endurance

The folding endurance or flexibility of the implants was determined by repeatedly folding the implants at the same place until it breaks. The number of times the implants folded without breaking as considered as folding endurance [23].

2.4.5. Tensile strength

The Tensile strength of the implants was determined by the Universal strength testing machine. It consists of two load cell grips, the lower one is fixed and the upper one is movable. The test implants of specific size (4.5x1 cm^2) were fixed between these cell grips and force was gradually applied till the implants breaks [20]. Tensile strength was calculated by using formula (Equation 1):

$$\text{Tensile strength} = \frac{\text{Force at break (N)}}{\text{Initial cross sectional area of implants } (mm^2)}$$

……(Equation 1)

2.4.6. Percentage moisture loss

The percentage moisture loss test was carried out to check physical stability or integrity of the implants. 6 Implants of known weight and size (8x2 mm^2) were placed in a desiccator containing anhydrous calcium chloride. After 3 days, the implants were taken out, re-weighed and calculated percentage moisture loss using the following formula (Equation 2): [20, 24]

$$\%\text{Moisture loss} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \text{ X } 100$$

…

……(Equation 2)

2.4.7. Drug Content Uniformity

The drug-loaded implants of known size (8x2 mm^2) was taken in 10 ml of acetic acid 1% $_{V/V}$ and crushed until dissolved. The dispersion was kept overnight in dark place. The dispersion was filtered. Then 0.1 ml of the filtered solution was diluted to 10 ml with phosphate buffer pH 6.8 in a 10 ml volumetric flask. Drug concentrations were determined by taking 6 readings, using a UV-Visible Spectrophotometer at 210 nm. (UV1800, Shimadzu, Japan) [9, 25].

2.4.8. *In-vitro* drug release

The pH of gingival fluid lies in between 6.5 to 6.8. Phosphate buffer pH 6.8 solution were used which were similar to the pH of saliva. Since the implants should be immobile in the periodontal pocket, a static dissolution method was adopted for the dissolution studies. Implants of size (8x2 mm^2) were taken separately into small test tubes sealed with aluminium foil containing 10 ml simulated saliva (pH 6.8) and kept at 37^{o}C. The temperature was maintained at 37^{o}C by keeping the test tube in dissolution apparatus with temperature control. The sample was withdrawn and replaced with fresh 1 ml of pH 6.8 at a predetermined time intervals up to 24 hours. The concentration of drug in the buffer was measured at 210 nm by using a UV-Visible Spectrophotometer. (UV1800, Shimadzu, Japan) [26, 27].

2.4.9. *In-vitro* antibacterial activity

The implants of size (5x5 mm^2) were taken for the study; 60 ml of nutrient agar media was prepared and sterilized at 15 lb pressure for 20 min in an autoclave. Under aseptic condition, 20 ml of nutrient agar media was transferred into sterile Petri plates. After solidification, 0.1 ml of microbial suspension of *S.aureus* of known concentration was spread on media. The implants were placed over the medium and the plates incubated for 48 hours at 37^{o}C. Then the zone of inhibition was measured [8, 19].

2.4.10. Short term stability studies

The drug loaded Dental implants were subjected to short term stability testing. The Dental implants were wrapped in aluminium foil and placed in petriplate which were kept in a stability chamber maintained at two different temperature 5 ± 3^{o}C, 40 ± 2^{o}C and 75 ± 5% RH for 45 days [11] after 45 the implants were evaluated for physicochemical parameters and *in-vitro* drug release.

3. RESULTS AND DISCUSSION

3.1. Drug polymer compatibility FT-IR study

The drug polymer compatibility was studied by FT-IR Spectroscopy (BRUKER ALPHA E). FT-IR spectrum for Clindamycin hydrochloride, physical mixture of drug-polymers and CDH 9 are shown in Table: 2 Figure: 1-3.

It indicates that pure drug functional groups peaks were present in all the physical mixture and formulation there is no much deviation in the peak position. Hence it shows that polymer were compatible with the drug.

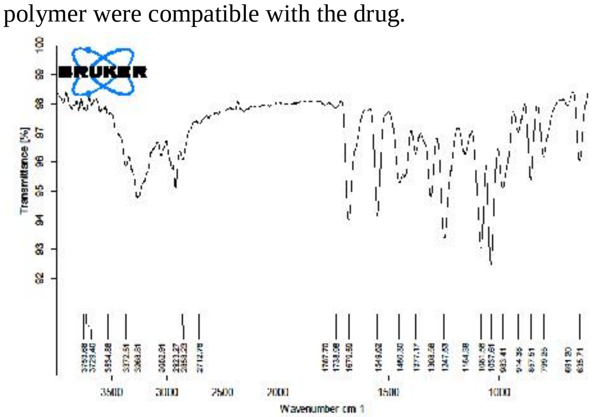

Fig 1: IR spectra of Clindamycin hydrochloride

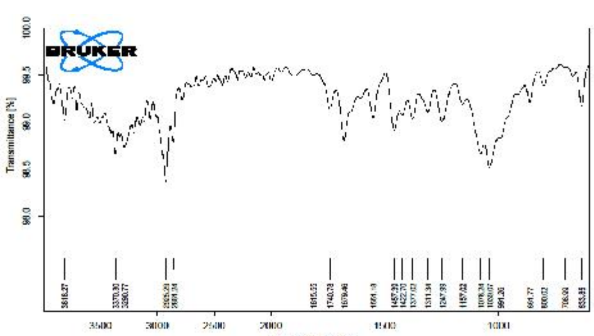

Fig 2: IR spectra of physical mixture of drug-polymers

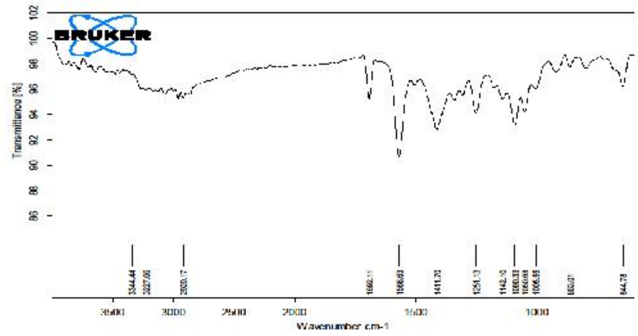

Fig 3: IR spectra of CDH 9

Table 2: Major peaks of Clindamycin hydrochloride in IR spectra

Functional Groups	Frequency of pure drug (cm^{-1})	Frequency of Physical mixture (cm^{-1})	Frequency of CDH 9 (cm^{-1})
O-H Str	3372	3370	3344
N-H Str	3268	3290	3227
C-H Str	2923	2925	2920
C=O Str	1679	1679	1692
CH=CH Str	1549	1551	1568
C-O-C Str	1154	1157	1142
N-CH$_3$ Str	1081	1078	1090
S-CH$_3$ Str	1037	1039	1050
C-Cl Str	857	861	863

3.2. Differential scanning calorimetry

DSC thermogram of Clindamycin hydrochloride exhibited sharp endothermic peak at 141^{o}C, 170^{o}C. Physical mixture of drug-polymers shows peak at 143^{o}C, 171^{o}C in DSC thermogram. This indicated that there is no interaction between drug and polymer. Shown in Figure: 4, 5

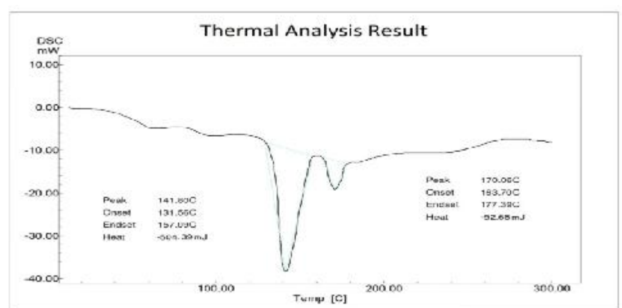

Fig 4: DSC Thermogram of Clindamycin hydrochloride

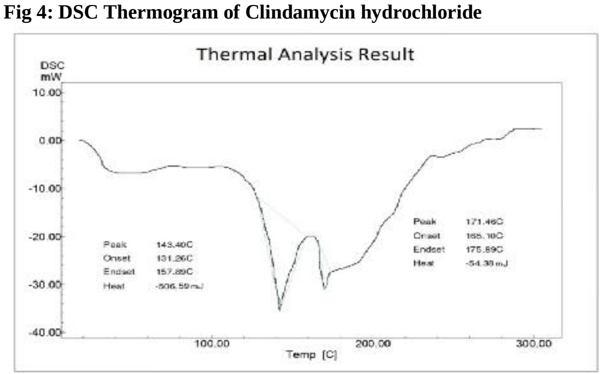

Fig 5: DSC Thermogram physical mixture of drug-polymers

3.3. Scanning electron microscopy

The SEM of drug loaded implants reveals that the surface of implants was smooth and free from air bubbles. The results are shown in Figure: 6.

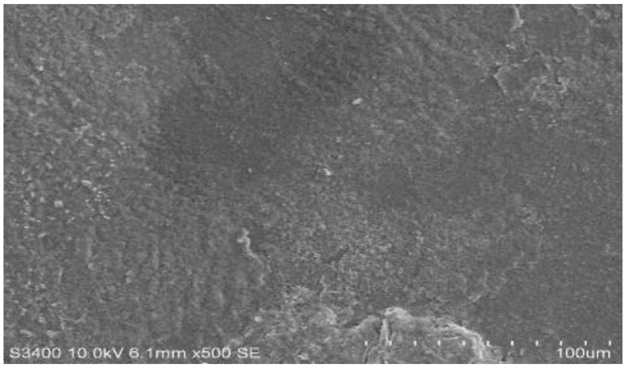

Fig 6: SEM images Drug loaded implants

3.4. Weight uniformity

Drug loaded implants (8x2 mm^2) were tested for uniformity and the results are shown in Table: 3 the results indicated that the implants are uniform in weight. Weight uniformity ranging from: 4.18 mg to 8.28 mg.

3.5. Thickness

Drug loaded implants were tested for thickness and the results are shown in Table: 3 the results indicated that the implants are uniform in thickness. Thickness ranging from: 0.318 mm to 0.542 mm.

3.6. Surface pH

The Surface pH of all formulation were in range of 6-7 is close to the neutral pH, these implants are suitable to be inserted into the periodontal pocket with no irritation to the mucosa. The results are shown in Table: 3.

Table 3: Weight uniformity, thickness, surface pH

Formulation code	Weight Uniformity (mg) $\bar{X}$ ± RSD (%)	Thickness(mm) $\bar{X}$ ± RSD (%)	Surface pH $\bar{X}$ ± RSD (%)
CDH 1	4.18±0.93	0.318±0.25	6.6±7.74
CDH 2	7.25±0.88	0.518±0.32	6.8±5.97
CDH 3	5.11±0.70	0.428±0.41	6.5±8.42
CDH 4	8.23±0.86	0.523±0.43	6.5±8.42
CDH 5	6.07±0.89	0.455±0.24	6.8±5.97
CDH 6	7.48±0.98	0.475±0.38	6.5±7.74
CDH 7	8.15±0.86	0.542±0.15	6.6±8.42
CDH 8	6.39±1.18	0.452±0.31	6.5±8.42
CDH 9	5.85±0.61	0.424±0.24	6.8±5.97
CDH 10	6.09±0.79	0.463±0.18	6.5±8.42
CDH 11	7.13±1.34	0.494±0.47	6.6±7.74
CDH 12	6.81±1.63	0.456±0.12	6.6±7.74

3.7. Folding endurance

The folding endurance was more than 250 times which reflects the flexibility of the implants. The results are shown in Table: 4.

3.8. Tensile strength

Tensile strength was determined by universal material testing machine. The results are shown in Table: 4. Tensile strength ranging from: 1 N/mm^2 to 2.57 N/mm^2

3.9. Percentage moisture loss

Percentage moisture loss was done for drug loaded implants and results are shown in Table: 4. Low moisture loss helps the formulation to remain stable and prevent from being completely dried and brittle. Percentage moisture loss ranging from: 7.16 to 10.72.

3.10. Drug content uniformity

Drug content uniformity test was carried out, in order to make sure about the uniform dispersion of drug in the implants. The results are shown in Table: 4 the results indicated that the drug was uniformly dispersed the procedure of preparing polymeric solution gives the reproducible results ranging from: 89.45% to 97.38%.

Table 4: Folding Endurance, Tensile Strength, Percentage Moisture Loss, Drug Content Uniformity

Formulation code	Folding Endurance $\bar{X}$ ± RSD (%)	Tensile Strength (N/mm^2) $\bar{X}$ ± RSD (%)	Percentage Moisture Loss $\bar{X}$ ± RSD (%)	Drug Content Uniformity (%) $\bar{X}$ ± RSD (%)
CDH 1	345±0.40	1.49	10.03±0.51	95.09±0.82
CDH 2	282±0.39	1	9.89±0.42	89.45±0.54
CDH 3	295±0.57	1.79	8.21±0.49	92.53±0.71
CDH 4	252±0.12	1.44	11.54±0.45	90.64±0.53
CDH 5	324±0.26	1.48	8.99±0.30	90.25±0.68
CDH 6	342±0.54	1.77	9.29±0.37	93.18±0.47
CDH 7	267±0.17	1.19	12.26±0.28	91.63±0.69
CDH 8	333±0.41	2.57	9.2±0.41	94.42±0.58
CDH 9	350±0.16	1.68	7.16±0.29	97.38±0.42
CDH 10	300±0.37	1.73	8.14±0.14	95.51±0.55
CDH 11	285±0.25	1.38	10.72±0.47	93.12±0.63
CDH 12	340±0.28	2.21	9.91±0.50	96.19±0.77

3.11. *In-vitro* drug release

A static dissolution method was adopted for the dissolution studies. Phosphate buffer pH 6.8 was used which were similar to the pH of saliva. Since the implants should be immobile in the periodontal pocket.

The results of *in-vitro* drug release are shown in Table: 5 and Figure: 7 Cumulative percentage of formulation ranges from 88.59% to 95.14% Formulation CDH 9 with 95.14% drug release and from graph it shows maximum drug release compare to other formulation

Table 5: *In-vitro* drug release of Clindamycin hydrochloride Dental implants from CDH 1 to CDH 12 in Phosphate buffer pH 6.8

Time (hrs)	% Drug Release X̄± RSD (%) (n=6)											
	CDH 1	CDH 2	CDH 3	CDH 4	CDH 5	CDH 6	CDH 7	CDH 8	CDH 9	CDH 10	CDH 11	CDH 12
0	0	0	0	0	0	0	0	0	0	0	0	0
1	13.22±0.20	8.61±0.26	11.54±0.41	10.35±0.12	9.48±0.12	12.25±0.19	7.88±0.23	11.31±0.31	15.22±0.26	11.54±0.36	10.23±0.39	14.11±0.28
2	21.41±0.11	16.35±0.39	21.13±0.29	19.31±0.16	17.53±0.36	23.14±0.31	16.03±0.48	19.09±0.27	29.01±0.03	18.19±0.48	17.39±0.16	27.42±0.12
3	29.72±0.15	23.86±0.15	30.69±0.35	28.58±0.45	25.51±0.02	32.11±0.48	23.62±0.11	27.15±0.14	40.75±0.34	26.43±0.17	25.05±0.23	38.18±0.25
4	38.51±0.43	32.49±0.24	38.35±0.28	37.04±0.31	32.19±0.48	41.27±0.26	29.49±0.5	34.22±0.50	52.46±0.12	32.79±0.21	31.53±0.49	47.23±0.39
5	47.36±0.34	39.33±0.37	47.83±0.29	46.9±0.19	40.82±0.14	49.01±0.03	36.23±0.45	42.31±0.25	63.72±0.28	39.22±0.37	37.74±0.07	56.06±0.41
6	55.68±0.12	47.54±0.22	53.65±0.30	55.27±0.25	49.36±0.43	57.43±0.18	44.29±0.28	51.14±0.06	71.02±0.36	46.13±0.45	43.36±0.01	64.26±0.08
7	62.09±0.38	56.57±0.31	59.29±0.14	64.36±0.10	58.01±0.05	65.06±0.25	50.18±0.46	62.07±0.21	77.15±0.05	53.20±0.50	49.43±0.36	70.02±0.27
8	69.33±0.29	63.28±0.19	66.42±0.46	72.10±0.25	65.27±0.16	73.47±0.42	58.37±0.19	68.12±0.45	82.27±0.23	60.04±0.19	56.72±0.21	75.81±0.43
9	76.56±0.32	70.66±0.17	71.79±0.27	77.42±0.43	73.66±0.39	79.19±0.19	63.16±0.34	74.56±0.16	85.09±0.11	68.22±0.23	63.60±0.42	79.23±0.18
10	81.47±0.41	76.39±0.25	78.52±0.19	82.15±0.37	78.01±0.42	82.61±0.38	69.31±0.21	79.28±0.21	87.13±0.49	75.13±0.12	71.48±0.27	83.52±0.22
11	85.53±0.47	80.37±0.36	83.4±0.28	85.03±0.42	82.46±0.09	86.47±0.41	75.87±0.49	83.11±0.47	89.21±0.31	81.29±0.43	77.59±0.31	86.14±0.40
12	87.92±0.13	84.75±0.11	85.93±0.35	87.16±0.18	84.45±0.28	88.21±0.23	79.01±0.17	85.61±0.23	90.27±0.48	86.41±0.04	82.09±0.19	88.25±0.39
16	90.4±0.44	85.91±0.45	88.85±0.21	89.03±0.09	86.21±0.17	90.13±0.15	82±0.09	87.28±0.35	92.1±0.12	91.12±0.11	86.53±0.48	90.36±0.18
20	92.55±0.09	87.47±0.21	90.34±0.36	90.15±0.47	87.16±0.16	91.24±0.04	84.61±0.27	88.49±0.39	93.42±0.54	92.09±0.33	87.82±0.31	92.18±0.41
24	93.07±0.24	88.59±0.17	91.12±0.14	91.07±0.32	88.63±0.02	92.18±0.26	85.05±0.13	90.17±0.11	95.14±0.18	93.28±0.26	89.11±0.05	94.12±0.16

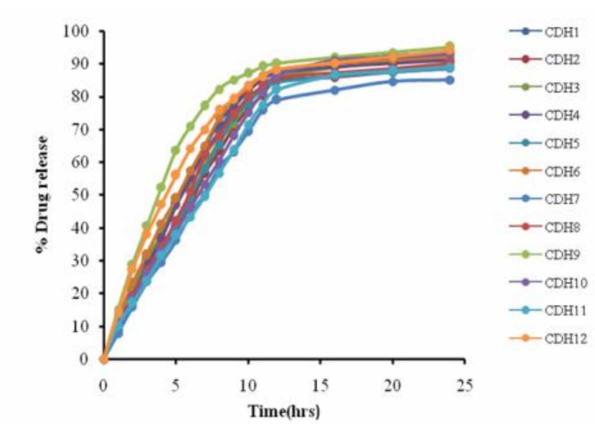

Fig 7: Graph of *in-vitro* drug release profile of CDH 1 to CDH 12

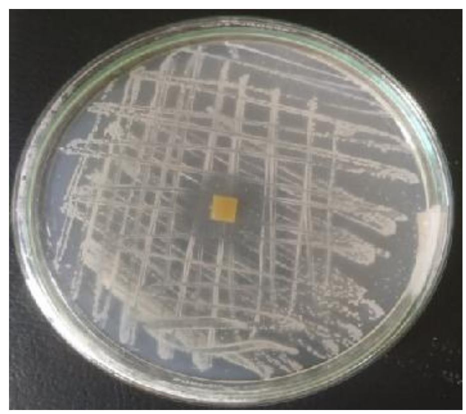

Fig 8: Zone of Inhibition of Clindamycin hydrochloride Dental implant CDH 9

3.12. *In-vitro* antibacterial studies

In-vitro Antibacterial Studies was performed on the most satisfactory Formulation CDH 9 using microbial strains of *S.aureus.* The results are shown in Table: 6 Figure: 8

Table 6: *In-vitro* Antibacterial study of Clindamycin hydrochloride Dental implants

Formulation code	Zone of Inhibition (mm) at 48hrs
CDH 9	22 mm

3.13. Short term stability studies

The short-term stability study was carried out as per ICH Guidelines on the most satisfactory Formulation CDH 9 at two different temperature 5 ± 3^{o}C, 40 ± 2^{o}C and 75 ± 5% RH for a period of 45 days. At fixed time, the formulation was evaluated after for their physicochemical parameters and *in-vitro* drug release. There was no significant difference in the physicochemical parameters and *in-vitro* drug release with the initial results. The results are shown in Table: 7, 8 this indicates that the prepared Dental implants were found to be stable.

Table 7: Physicochemical evaluation of formulation CDH 9 after stability studies (5 ± 3ºC)

Sl. No.	Parameters	Before stability testing	After stability testing
1.	Weight Uniformity	5.85±0.61	5.83±0.79
2.	Thickness	0.424±0.24	0.423±0.36
3.	Surface pH	6.8±5.97	6.8±7.74
4.	Folding Endurance	350±0.16	349±0.46
5.	Percentage Moisture Loss	7.16±0.29	7.18±0.54
6.	Drug Content Uniformity	97.38±0.42	97.01±0.45
7.	Drug Release at 24th hours	95.14±0.18	95.02±0.14

Table 8: Physicochemical evaluation of formulation CDH 9 after stability studies (40 ± 2ºC)

Sl. No.	Parameters	Before stability testing	After stability testing
1.	Weight Uniformity	5.85±0.61	5.84±0.57
2.	Thickness	0.424±0.24	0.423±0.66
3.	Surface pH	6.8±5.97	6.8±7.74
4.	Folding Endurance	350±0.16	349±0.11
5.	Percentage Moisture Loss	7.16±0.29	7.19±0.34
6.	Drug Content Uniformity	97.38±0.42	97.25±0.19
7.	Drug Release at 24th hours	95.14±0.18	95.07±0.27

4. CONCLUSION

Dental implants containing antibacterial drug Clindamycin hydrochloride were prepared by solvent casting technique. FT-IR spectra and DSC revealed that there was no interaction between the drug and polymer. SEM studies indicated that the prepared implants are having smooth surface. Evaluation parameters like Thickness, Folding Endurance, Tensile Strength indicates that the Dental implants were mechanically stable. Weight uniformity and Drug content uniformity were found to be uniform in all the implants. *In-vitro* drug release studies shows that release from the Dental implants gets successfully retarded for over 24 hours. Based on the results obtained from the physicochemical parameters and *in-vitro* drug release CDH 9 was found to be best formulation. *In-vitro* Antibacterial study was carried for optimized formulation CDH 9 using bacterial stains of *S.aureus* the zone of inhibition was found effective. The optimized formulation was found to be stable in Short term stability studies according to ICH Guidelines Clindamycin hydrochloride is usually of higher dose and shorter half-life so it is formulated as Dental implants. Since the drug release occurred locally, it had high benefit to low risk ratio as compared to systemic administration, which is unacceptable due to, low benefit to high-risk ratio. Hence low dose site-specific implants, sustained effects are a better alternative to systemic therapy in treatment of periodontal diseases. By considering the results obtained from *in-vitro* and Stability studies, it can be suggested that there is further scope for the *in-vivo* and Pharmacokinetic Study.

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