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# Periodontal treatment by local drug delivery using resorbable Base materials; in vitro comparative study assessing drug delivery properties of cellulose acetate and alginate strips

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**ABSTRACT:**

**Periodontal diseases are characterized by microbial colonization of the pockets; the elimination of these microbes helps in achieving good prognosis along with the control of inflammation in the treatment of this disease and use of anti-microbials & anti inflammatory agents is an invaluable aid. The use of local drug delivery has been of added advantage over systemically given drugs, to date many local drug delivery vehicles were used which include drug incorporated Gels, resorbable microspheres etc but a very economical and effective drug delivery system was very much needed for wide spread use of this mode of drug delivery for treatment of periodontal infection, which happens to be the most prevalent cause of tooth loss. In this invitro study, the drug release patterns of two most economical and easily made resorbable base materials like sodium alginate and cellulose acetate strips incorporated with drugs most commonly used in treatment of Periodontitis like Metronidazole and Indomethacin (used as anti inflammatory agent)were evaluated, in salivary substitutes using spectrophotometer.**

**The release evaluations were performed at 1st hour, 2nd, 3rd, 4th, 5th, 24th and 48th hours, the temperature of the medium (salivary substitute) in which these strips were evaluated was maintained at 98°F using an electronically controlled conventional induction plate to mimic the normal body temperature.**

**The evaluation of release patterns showed that the onset of drug release (of either Indomethacin or the Metronidazole) was very quick from the sodium alginate and the near 100% release was achieved with both the drugs within 24 hours where as with cellulose acetate the onset of drug release was a little slower starting almost 2 - 3hrs later than sodium alginate and the release pattern was very slow achieving only approximately 67-69% after 48 hours.**

***Key words:*** ***Local drug delivery, Periodontitis, pocket, invitro, inflammation***

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## INTRODUCTION

Periodontitis is a multi-factorial disease affecting the tooth supporting structures, leading to the loss support of the affected tooth /teeth as a consequence of which the teeth become loose in their socket and finally leading to the tooth loss.

Primarily the etiological factors responsible for the occurrence of Periodontitis is bacterial plaque which accumulates and in time matures causing inflammatory changes in the supporting tissues of the tooth leading to the damage of alveolar bone, periodontal ligament and the cementum which finally leads to tooth loss, although primarily the bacterial plaque is implicated in this process, not all the people having plaque accumulations exhibit the similar kind of severity of the disease. This discrepancy in the disease severity in different people suggests that it is not the quantity of plaque which

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is responsible for the disease severity but in fact the quality of plaque dictates the nature and course of the disease(specific plaque theory). In the similar manner, the kind of immunological response exhibited by the host is also said to be the important factor in deciding the rate of disease progression(host response), so the nature of host response, age, rate of bone loss is also important when classifying Periodontitis as aggressive or chronic.

Whichever may the type of Periodontitis, the initiating factor always will be the bacterial plaque. Hence the treatment of this disease aims at removal of plaque from the tooth surfaces, which can be achieve by scaling and root planning (mechanical plaque control), or through the use of chemical plaque controlling agents (use of antibacterial agents), which control the growth of plaque or which reduce the pathogenic plaque organisms in the oral cavity there by reducing the bacterial load thus helping in the treatment of Periodontitis.

Although the mechanical plaque controlling methods are more effective in removal of bacterial plaque, the inaccessibility of the areas in which the plaque tends to accumulate and initiates the disease makes them ineffective in arresting the progression of the disease in areas such as furcations, narrow inter-dental spaces and distal most teeth hence when complete plaque control is anticipated it is prudent to practice chemical plaque controlling methods with mechanical plaque controlling methods.

When the issue of controlling the sub gingival plaque comes, the routine chemical plaque controlling methods which use chemicals in the form of mouth washes do not yield the intended results because of limited time of their presence in the oral cavity, thus the need of developing a method, which delivers the antibacterial agent in the sub gingival site for extended periods has led to the introduction of local drug delivery systems.

Several studies for controlling the sub-gingival plaque by local drug delivery have been published by other investigators. These methods, using hollow-fiber devices (Lindhe *et al,* 1979), acrylic resin strips (Addy *etal,* 1982), and monolithic fibers (Goodson *et al,* 1983), seem to be effective in changing the microflora in periodontal pockets and in reducing periodontal inflammation. For their routine use in the treatment of periodontal diseases, these methods require carriers of the drug to be administered and removal of the carrier at regular intervals after the release of the drugs. In the present study, resorbable base material (cellulose acetate & sodium alginate) are used to deliver antimicrobial & anti-inflammatory drugs directly into periodontal pockets. The purpose of this study was to investigate, *in vitro,* the drug releasing properties of these two resorbable bases.

## MATERIALS AND METHODS

### Preparation of drug-loaded films

The cellulose acetate films containing Metronidazole/ Indomethacin were prepared by the solvent evaporation technique, 50mg of cellulose acetate was dissolved in 5ml acetone and 350 mg of either of the active agents was dispersed in the cellulose acetate. These mixtures were poured in wax sheet containing grooves of specified dimensions, mounted on aluminum foil and evaporated at room temperature overnight. The films were then cut in a desired form to fit periodontal pocket anatomy. (5x5x1mm). The alginate strips were prepared by solution of known concentration (10%) along with the predetermined drug (Metronidazole/ Indomethacin) quantity, which was allowed to stand till free of air bubbles and then poured in a wax sheet containing grooves with specified dimensions mounted on clear glass plate, so that the solution spreads evenly on the surface. Then calcium chloride solution (10%) was poured over the solution alginate and the glass plate was allowed to stand till it polymerizes and forms a strip which is then cut into necessary sizes.

### The release studies

The release studies were carried out in 10 ml artificial saliva WET MOUTH (ICPA) for this purpose. Samples were taken at pre-determined time intervals t (hour) for **t (hour)** 0, 1, 2, 3, 4, 5, 24, 48. Determinations were carried out spectro-photometrically. The released amounts of Indomethacin, and Metronidazole were determined at 330, 334.5 nm, respectively, and the release profiles were plotted as a function of time.

## RESULTS

**TABLE –I: Concentration of Indomethacin released from Sodium Alginate and Cellulose acetate strips as function of time**

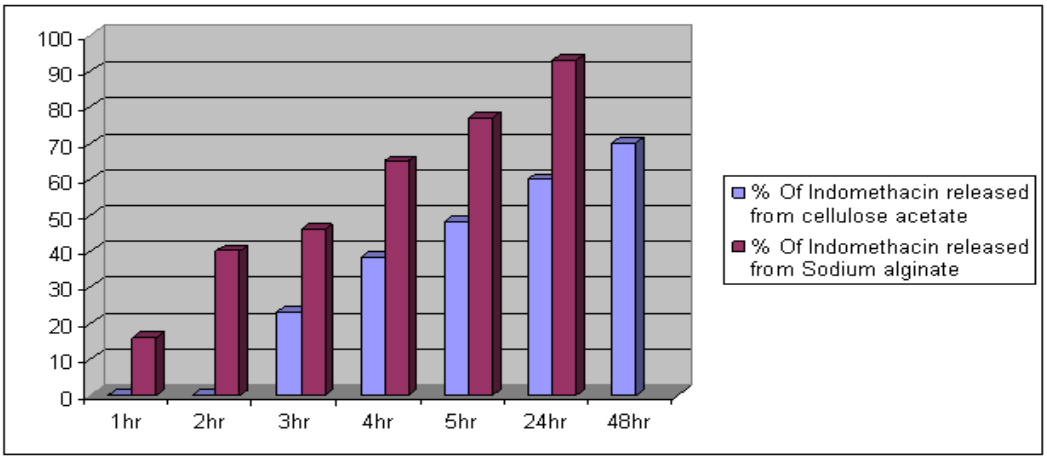
| Time(hrs) | Conc. of Indomethacin released from Sodium alginate | % Drug released | Conc. Of indomethacin released from cellulose acetate | % Drug released |
|---|---|---|---|---|
| 1 | 0.17 | 16 | 0 | 0 |
| 2 | 0.42 | 40 | 0 | 0 |
| 3 | 0.49 | 46 | 0.34 | 22 |
| 4 | 0.69 | 65 | 0.57 | 38 |
| 5 | 0.82 | 77 | 0.71 | 47 |
| 24 | 0.99 | 93 | 0.90 | 60 |
| 48 | - | - | 1.04 | 69 |

**TABLE-II: Concentration of Metronidazole released from Sodium Alginate and Cellulose acetate strips as function of time**

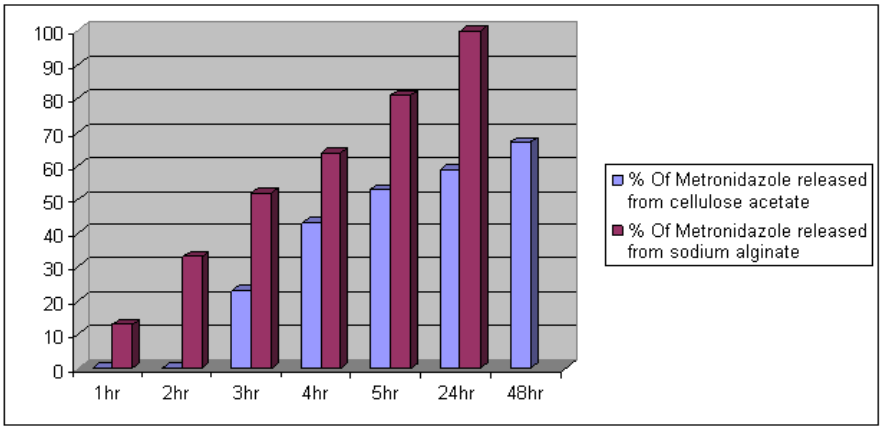
| Time(hrs) | Conc. of Indomethacin released from Sodium alginate | % Drug released | Conc. Of indomethacin released from cellulose acetate | % Drug released |
|---|---|---|---|---|
| 1 | 0.14 | 13 | 0 | 0 |
| 2 | 0.36 | 33 | 0 | 0 |
| 3 | 0.56 | 52 | 0.33 | 23 |
| 4 | 0.69 | 64 | 0.62 | 43 |
| 5 | 0.88 | 81 | 0.75 | 52 |
| 24 | 1.09 | 100 | 0.84 | 59 |
| 48 | - | - | 0.96 | 67 |

**Graph -I**

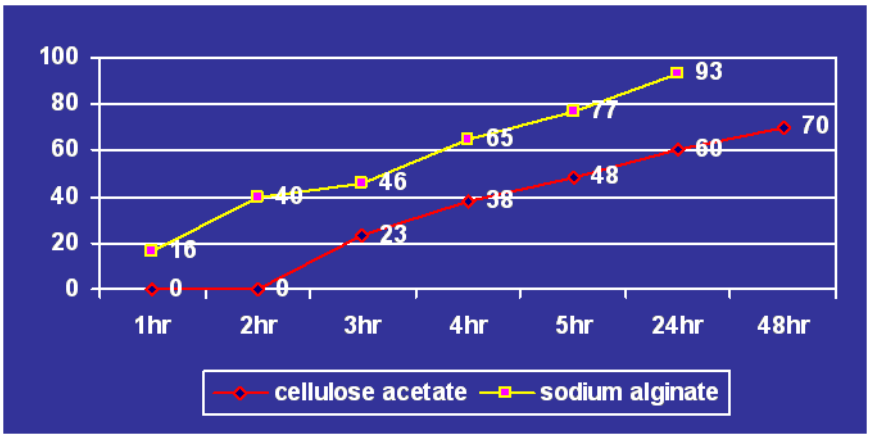
**Percentage of Indomethacin released from Cellulose acetate and Sodium alginate as function of time**



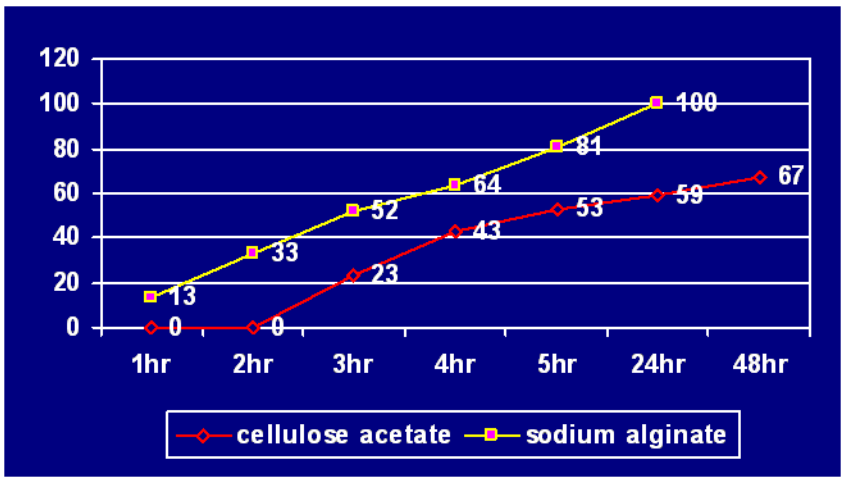
**Graph-II**
**% of Metronidazole released from Cellulose acetate & Sodium alginate as function of time**




**Graph- III**
**Time versus %of Indomethacin released from Cellulose acetate &Sodium alginate**




**Graph- IV**
**Time versus % of Metronidazole released from Cellulose acetate & Sodium alginate**



## DISCUSSION

Local drug delivery device exists in both resorbable or non-resorbable matrices both of which contain a drug reservoir and a limiting element that controls the rate of medicament release. This study was mainly carried out using resorbable bases such as cellulose acetate and alginate in order to see to what extent the drug release can be achieved and up to what period we can see such significant release. The bases are known for their water solubility and sustained release for extended periods (24-48 Hrs) and at the same time the drugs such as antibiotics and anti inflammatories can be incorporated into the bases with out any appreciable change in their chemical and medical properties, more over these bases are very well tolerated by oral tissues without any antigenic reaction.

Since there is substantial evidence that the main inflammatory mediators responsible for periodontal tissue destruction are also synthesized locally from the periodontal tissues (Garito et al 1995), it is important to control the concentrations of the inflammatory products in the GCF to limit the tissue destruction, so an anti inflammatory (Indomethacin) was also included in this evaluation study along with most widely antibiotic in treatment of Periodontitis that is Metronidazole.

In controlled release systems, it is generally difficult to obtain a constant release rate. In the present study, the release was rapid in the beginning period and the drug release was very rapid in sodium alginate leading to exhaustion of the reservoir even before 24 hrs, where as the release profile of the drug for cellulose acetate even though rapid initially, was maintained for more than 48 hrs. Most of the previous in vitro studies on release of drugs from local devices had investigated the materials in water (Addy et al 1982; Goodson et al 1983). To date there is no formulation of the artificial GCF preparation and considering the biochemical similarities as well as direct contacts between GCF and saliva, present study was performed using artificial saliva

### Limitations of the present study

- Although every effort has been made to simulate the in vivo conditions it is always impossible to obtain all the parameters to the point of exactness as exists in vivo
- Since the present study was carried out in artificial saliva, the effect of the drug on the bacterial flora, on the inflammatory mediators and on the host response was missing which needed an extensive future research in this direction to know the exact effect of these drugs
- This study was carried out only for a short period, hence further long term studies to confirm these results are highly warranted.

### Future prospects

The present study paves a path for future consideration to indigenously develop efficient and economically affordable local drug delivery devices to cater the needs of ever increasing periodontal patient community

## CONCLUSION

Based on the results of this study it is evident that the biodegradable drug delivery system as the one used in this study needs more refinement to deliver the drug at sustained concentration for prolonged periods while retaining the inherent benefits of the biodegradability.

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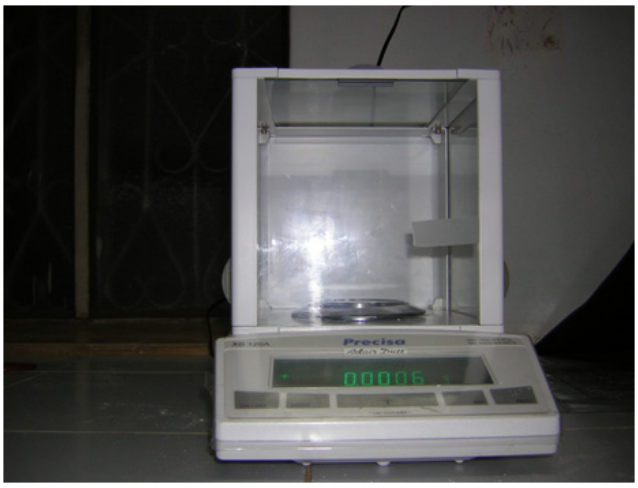
## APPENDIX- I

SPECTROPHOTOMETER


## APPENDIX-II

DIGITAL ELECTRONIC BALANCE

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