In vitro release of tinidazole from polyvinyl alcohol and polvinylpyrrolidine strips- local drug delivery system to treat periodontal pockets
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Abstract
Background: Local drug delivery systems have been investigated in the release of antimicrobials since decades to treat periodontal pockets in periodontal diseases. Aims: The purpose of this in-vitro study is to formulate polyvinyl alcohol strips containing tinidazole. Materials & Methods: Polyvinyl alcohol films containing tinidazole were prepared by dissolving polyvinyl alcohol and polyvinyl pyrrolidone powder in water and were slightly warmed on a water bath. The polymeric solution containing tinidazole was then poured on to rectangular slab designed glass molds and was kept overnight with inverted funnel to check evaporation. The release of the drug was analyzed by UV spectrophotometer. Results: The PVA strips had good content uniformity, thickness and folding endurance. Highest level of tinidazole was released during the first 24 h period. Therapeutic levels of the tinidazole continued to be released during the subsequent 9 days period and were shown to be biologically active. Conclusion: It can be concluded that PVA strips containing Tinidazole can be used as local drug delivery system.

Key Words: Local drug delivery; polyvinyl alcohol strips; tinidazole

Introduction
Local delivery systems offer the advantages of higher concentrations at the target site with reduced dosage, fewer applications. Polyvinyl alcohol (PVA) has been an important industrial dispersion stabilizer for decades and was first used in the 1930s in Germany as a surfactant in vinyl acetate latex stabilization. PVA films have been used in transdermal drug delivery system in vivo where in as shown promising effects in the release of drugs. Tinidazole has wide application in medical field as it is effective in the treatment of trichomianiasis, anaerobic gynecological infections, and dysenteric disorders like anaerobic liver abscess, acute amoebiasis, chronic amoebiasis and giardiasis, as a prophylactic agent in elective surgery of colon and rectum and in anaerobic wound infection. In dentistry, Tinidazole is found to be effective, as a prophylactic agent in surgery of impacted 3rd molar pericoritis, odontogenic cysts, in acute and chronic periodontal disease. Tinidazole a close analogue of metronidazole has fewer side effects, no active metabolites, and its serum half-life is approximately twice that of metronidazole. The effect of local application of Tinidazole has been evaluated through various local drug delivery systems. The purpose of this in vitro study is to find out the efficacy of polyvinyl alcohol strips containing tinidazole as local drug delivery systems which can be applied to treat periodontal pockets.

Materials & Methods
The present study was conducted in the department of pharmaceutics in J.S.S.Pharma College Mysore. In this study an attempt is made for developing dental implants from monolithic films of PVA and PVP incorporating Tinidazole as a model drug. The PVA, PVP and Propylene Glycol were of analytical grade and purchased from Sigma Aldrich and used as procured. Tinidazole was gift sample from Micro labs Pvt. Ltd., Bangalore.

The formulation of monolithic film of Tinidazole as follows: Ingredients: PVA 12% w/w, PVP – 3% w/w , Plasticizer- (Propylene Glycol) 30% of polymer, Tinidazole 10 mg, Purified water- QS.

PVA was dissolved in water, slowly by adding the powder and was slightly warmed on a water bath so as to hasten the dissolution of polymer. PVP was dissolved in water in another beaker. Both the polymer solutions were mixed and kept on magnetic stirrer with continuous stirring. Care was taken to avoid air entrapment. Tinidazole was added slowly to the polymer solution with constant stirring. The polymeric solution containing drug was then poured on to rectangular slab designed glass moulds and was kept overnight with inverted funnel to check evaporation. The films were cut into 1 cm of each containing 10 mgs of tinidazole and were taken up for further investigations. Tinidazole dental implants were formulated; Thickness, content uniformity, folding endurance and In vitro release studies, of these dental implants were evaluated.

Thickness of the implants: Thickness of the implants is important parameter as it could give the information about the uniform distribution of tinidazole in it. To measure the thickness, 10 numbers of 1cm 2 films was held together in the digital screw gauge (Mitotoyo, Japan) and the
thickness was measured and the obtained thickness was divided by 10 to get the thickness of single film.

Content Uniformity: In order to ascertain that tinidazole is uniformly distributed throughout the film, content uniformity test is carried out on 10 mm dental implant containing 10 mgs of drug were cut and dissolved in 10 ml of isotonic saline buffered saliva (IPBS) pH 7.2.

From the resulting solution 0.1 ml of solution is diluted to 10 ml to get a concentration of 10 mcg of and the absorbance was measured at 318 nm using UV Visible Spectrophotometer (UV-1601 Shimadzu, Japan).

Folding Endurance PVA strips: The prepared PVA Strip is folded at the same point several times till it gets cut. The number of times the strip is folded is taken as its folding endurance which gives the information on the flexibility and tensile strength of the strip.

In Vitro release of drug from PVA strips: Set of 3 PVA strips containing tinidazole all of known weight, which were placed separately into small 1.5 m test tubes containing 1 ml of distilled water. The tubes were sealed and incubated at 37oC for 24 hours in temperature controlled incubator (Thermolab, India). The water was then pipetted off and replaced with an additional 1 ml of distilled water. Employing the calibrated concentration facility of a double beam UV spectrophotometer, the concentration of tinidazole in water removed from around each strip was measured directly at 253 nm using UV Visible Spectrophotometer (UV-1601 Shimadzu, Japan). Background absorbance at this wavelength was determined. The procedure was continued over 10 consecutive days.

**Results**

The content uniformity of the PVA Strips revealed that Tinidazole was uniformly distributed in the strip and it was found to be 9.85 ± 0.125 mg. It was found that the prepared strips had uniform thickness of 114 ± 0.034 µm except for some trial film which were not uniform. The thickness of the film may vary if the polymeric solution in the mold is kept non-uniform surface (Table 1).

**Discussion**

The concept of local drug delivery system was investigated by Bethamann, later on Goodson et.AL 1979, developed and introduced the administration of tetracyclines into the periodontal pockets via hollow dialysis tubes.(6) A number of non-degradable and biodegradable materials, as local drug delivery systems have been currently used to treat periodontal pockets.(7) Till to date use of PVA in treating periodontal pocket is very minimal. Use of tinidazole in local drug delivery is less compare to other drugs, hence there is scanty literature, which promoted us to take tinidazole.

The PVA Strips showed good folding endurance for nearly 250 times indicating the strips are very flexible and has good tensile strength and can be easily implanted. In vitro drug release pattern was analyzed by using spectrophotometer, and the release pattern was accordance to the study conducted by Addy.(8) Highest levels (85 ± 0.082 %) of the antibacterial agents was released during the first 24h period. The percent drug release decreased gradually upon time up to 10th day. Therapeutic levels of the drug continued to be released during the subsequent 9 day period and were shown to be biologically active; Since PVA is a biosorbable, biocompatible, the release of the drug was by diffusion which was similar to the study conducted on transdermal drug delivery system in vivo by Jain G.K.et.al.(9)The advantage of using tinidazole over other nitro-imidazole group of drugs is due to its serum half-life is approximately twice and dosage is convenient. This in vitro study described the efficacy of PVA strips containing Tinidazole as a local drug delivery system which can be applied in treating periodontal pocket.

**Conclusion**

With these short term studies and results, it can be concluded that PVA strips containing Tinidazole can be used as local drug delivery system. Further long term in vivo studies have to be conducted to throw more light on PVA strips as local drug delivery system.

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