How to Cite:

Modern drug delivery formulations of potential anti-cancer herbal product

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Abstract---Objectives: The objective of the present work is to formulate and evaluate lozenges of potassium salt of curcumin extract for the anticancer activity that delivers drug into buccal cavity. It aids in the management of oxidative and inflammatory conditions, metabolic syndrome, arthritis, anxiety, and hyperlipidaemia. Curcumin lozenges were prepared for studying anticancer activity. Method: Solid dispersion of potassium curcuminate was prepared using β-cyclodextrin to enhance the solubility of potassium Curcuminate. The prepared solid dispersion of potassium Curcuminate was analysed for solubility enhancement. Curcuminate lozenges were then formulated with Potassium curcuminate, liquid glucose, sucrose and corn syrup by heat, and congealing technique. The prepared lozenges were evaluated for drug-excipient incompatibility study, colour, odour, taste and hardness. Results: The results of the compatibility study showed that there was no interaction between the selected drug and excipients. In-vivo studies of the lozenges were optimized based on in in-vitro drug release, drug Stability studies revealed that the formulation was stable Potassium curcuminate having greatest anticancer activity 85% towards prostate cancer cell, 80% towards liver cancer cell, and average of 92% towards colon cancer cell compared to curcumin and standard anticancer drugs like 5-Fu, Mito-C and Paclitaxel. Conclusion: From the present work, it was concluded that the potassium salt of Curcumin lozenges can be considered as a suitable delivery system for the treatment variety of Cancer.

Keywords---oral route, cancer, anticancer, tumor, normal cells, curcumin.
Introduction

Amongst the various routes of delivery, oral route is perhaps the most preferred to the patient and the clinician alike. However, peroral administration of drugs have disadvantages such as hepatic first pass metabolism and enzymatic degradation within the gastrointestinal tract, that prohibit oral administration of certain classes of drugs. The oral mucosa consists of an outermost layer of stratified squamous epithelium, which is covered with mucous and consists of stratum distendum, stratum filamentosum, stratum suprabasale and stratum basale. The area below the basal lamina is covered with lamina propria and submucosa. The epithelium serves as the mechanical barrier that protects underlying tissues, whereas the lamina propria provides a mechanical support and also carries the blood vessels and nerves. Some regions of the oral mucosa are keratinized. The oral mucosa in general is somewhat leaky epithelia intermediate between that of the epidermis and the intestinal mucosa. It is estimated that the permeability of the buccal mucosa is 4-4000 times greater than that of skin. As indicative by the wide range in this reported value, there are considerable differences in permeability between different regions of the oral cavity because of the diverse structures and functions of different oral mucosae.

The oral mucosa in general is somewhat leaky epithelia intermediate between that of the epidermis and the intestinal mucosa. It is estimated that the permeability of the buccal mucosa is 4-4000 times greater than that of skin. As indicative by the wide range in this reported value, there are considerable differences in permeability between different regions of the oral cavity because of the diverse structures and functions of different oral mucosae. In general, the permeability of the oral mucosae decreases in the order of sublingual greater than buccal and buccal greater than palatal. This rank order is based on the relative thickness and degree of keratinization of these tissues, with the sublingual mucosa is relatively thin and non-keratinized, the buccal thicker and non-keratinized, and palatal is intermediate in thickness but keratinized. There are two permeation pathways for passive drug transport across the oral mucosa: paracellular and transcellular routes. Permeants can use these two routes simultaneously, but one route is usually preferred over the other depending on the physiochemical properties of the diffusant. Since the intercellular spaces and cytoplasm are hydrophilic in character, lipophilic compounds would have low solubilities in this environment. The barriers such as saliva, mucus, membrane coating granules, basement membrane etc retard the rate and extent of drug absorption through the buccal mucosa.

The main penetration barrier exists in the outermost quarter to one third of the epithelium. In non-keratinized epithelia, the accumulation of lipids and cytokeratins in the keratinocytes are less evident and the change in morphology is far less marked than in keratinized epithelia. The mature cells in the outer portion of non-keratinized epithelia become large and flat retain nuclei and other organelles and the cytokeratins do not aggregate to form bundles of filaments as seen in keratinizing epithelia. Although the superficial layers of the oral epithelium represent the primary barrier to the entry of the substances from the exterior, it is evident that the basement membrane also plays a role in limiting the connective tissue. A similar mechanism appears to operate in the opposite...
direction. The charge on the constituents of the basal lamina may limit the rate of penetration of lipophilic compounds that can traverse the superficial epithelial barrier relatively easily. The epithelial cells of buccal mucosa are surrounded by the intercellular ground substance called mucus with the thickness varies from 40µm to 300 µm. Though the sublingual glands and minor salivary glands contribute only about 10% of all saliva together they produce the majority of mucus and are critical in maintaining the mucin layer over the oral mucosa. The mucosal surface has a salivary coating estimated to be 70µm thick which act as unstirred layer.

Within the saliva there is high molecular weight mucin named that can bind to the surface of the oral mucosa so as to maintain hydration, provide lubrication, concentrate protective molecules such as secretory immunoglobulins, and limit the attachments of micro-organisms. Administration of a drug via buccal mucosa to the systemic circulation is defined as buccal delivery. Despite, the buccal mucosa is significantly less permeable than the sublingual mucosa and usually not able to provide rapid drug absorption or good bioavailability, it is relatively more permeable than skin and also offers other advantages over alternative delivery routes. Alternatively drug released from medical chewing gum and lozenges, if does not get absorbed through oral cavity membrane than can be swallowed and entered in the stomach in a dissolved or a dispersed form in saliva. Thus the drug would be available to gastro intestinal tract for absorption. Alternatively drug released from medical chewing gum and lozenges, if does not get absorbed through oral cavity membrane than can be swallowed and entered in the stomach in a dissolved or a dispersed form in saliva. Thus the drug would be available to gastro intestinal tract for absorption.

The frequency of a particular cancer may depend on the gender factor. Skin cancer is the most common type of malignancy for both men and women, the second most common type in men is prostate cancer and in women, the breast cancer. Its frequency does not equate to cancer mortality. Skin cancers are often curable. Lung cancer is the leading cause of death in both men and women.

**Materials and Method**

**Materials**

Potassium di Hydrogen Othophosphate was obtained from Qualigens Fine Chemicals, Sodium Hydroxide was gotten from Qualigens Fine Chemicals, Liquid Glucose from Laxmi Confectionaries Ltd, Akola, and Curcumin from CHR-Hansen Pvt Ltd, Mumbai

**Drug Profile**

![Curcumin chemical structure](image)

Figure 1. Curcumin chemical structure
Synonym: Diferuloyl Methane  
Molecular Weight: 368.37  
Description: Curcumin occurs as orange yellowish powder. It is practically insoluble in Water\textsuperscript{17}.

Method

Preparation of potassium curcuminate salt: \textsuperscript{18}

Curcumin diferuloyl methane is insoluble in water. It is considered worthwhile to prepare water soluble alkali phenates of curcumin which might possess enhanced activity compared to curcumin. The procedure followed to prepare alkali salt of the curcumin is as follows: Curcumin was added to alcoholic potassium hydroxide (1:2 moles respectively) and stirred to homogeneous thin paste which soon liquefied to a deep red solution. After adding an excess of about 5\% curcumin and thorough stirring, the liquid was dried in a current of air at 400 C. The dried mass was than dissolved in minimum quantity of cold water and filtered under reduced pressure. The filtrate containing the potassium phenates were evaporated to dryness as above and finally in vacuum desiccators to constant weights. Solid dispersion of potassium curcuminate was prepared using \(\beta\)-cyclodextrin to enhance the solubility of potassium Curcuminate.

Cell lines and cell culture preparation\textsuperscript{19}

PC-3, HEP-2, A-549, 502713, HCT-15 and SW-620 cell lines were obtained from Indian Institute of Integrated Medicine, Jammu. Cells were cultured in 2-3 ml of 0.05\% trypsin-EDTA. And addition of 10 ml of 5\% serum containing RPMI 1640 medium.

In vitro dissolution studies for Potassium curcuminate\textsuperscript{20}

Lozenges were placed in the pot of the dissolution apparatus. Paddles were used as rotating device at the speed of 50 rpm and the temperature was maintained at 37.0±10\textdegree C throughout the experiment the dissolution process was carried out using 6.4 pH phosphate buffer. Aliquots 5mL of samples at predetermined time intervals and were replaced with fresh dissolution fluid to maintain sink conditions. The samples withdrawn were studied for their absorbance at on spectrophotometer

Formulation of Lozenges\textsuperscript{21}

Accurate amount of potassium curcuminate was transferred to a beaker, and was mixed with accurately weighed lactose. Liquid glucose, sucrose and corn syrup were weighed and mixed thoroughly, then passed through sieve no. 60. Which produces a mass of the required consistency? The mass was rolled on lozenge board and cut to required size. The lozenges were dried in a hot air oven. Details are mentioned in table no. 1. Table-1 Formulation of Lozenges
Evaluation of Lozenges

Stability testing

The purpose of this testing is to determine the physical and chemical stabilities of medicament, flavour, candy base and colour both under accelerated temperature and humidity conditions and at ambient storage conditions. This testing will enable the formulator to predict the acceptable shelf life of the product in a relatively short period of time and make changes as required to eliminate any incompatibilities that may influence product stability. Elevated temperature and elevated humidity testing: Elevated temperature and elevated humidity testing is initiated as soon as product is manufactured. Product should be tested at elevated temperatures and elevated humidity conditions. Testing conditions generally utilized by the product development laboratory include 250°C at 80% relative humidity for 6-12 months, 370°C at 80% humidity for 3 months, and 250°C at 70% relative humidity for 6-12 months. The elevated humidity studies are carried out both at constant humidity and in humidity cabinets with day and night cycling. Elevated humidity tests are vital for ascertaining medicament stability and candy stickiness including surface graining characteristics.

Physical stability

Concurrent with the chemical stability evaluation, a physical stability study is carried out on the product in order to determine what factors will detract from organoleptic appeal of the product and how long these changes will take place to occur. A routine physical stability evaluation includes:

- **Color:**
  Lozenges are checked for the color stability by keeping them in direct sunlight and at elevated temperatures to determine if the colours are light fast, also changes occurring due to presence of medicaments are to be evaluated. Table no. 2.
- **Odour:**
  Changes in the odour of flavours at elevated temperature are evaluated by sealing the lozenges in glass bottles and determining if any odour is there.
- **Taste:**
  The product is tasted and compared to production controls in order to determine if any flavour change have occurred. Many small flavour changes that cannot be detected via gas–liquid chromatography can be ascertained when lozenge is tasted. Any change in the surface texture is also evaluated during the taste evaluation. Result mentioned in table no.2.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Appearance</th>
<th>Colour</th>
<th>Dissolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>First day 4°C</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Room Temp</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>37°C</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>50°C</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

Table 2

Study for stability of potassium curcuminate Lozenges
Weight variation test

Twenty Lozenges were taken and their weight was decided exclusively and all things considered on a computerized weighing balance. The typical load of one not set in stone from the system weight. The weight variety test would be a agreeable strategy for deciding the medication content consistency. The percent deviation was determined utilizing the accompanying equation. The outcomes are introduced in

\[
\% \text{ Deviation} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100
\]

Hardness

Compressed tablet lozenges are tested for proper hardness using Pfizer hardness tester. The force required to penetrate the lozenge is used as measure of chewiness, surface harness and stability. Results are mentioned in table no. 3

Lozenges thickness

Lozenges thickness is a significant trademark in repeating appearance. Twenty Lozenges were taken and their thickness was recorded utilizing Digital Micrometer. The typical thickness for Lozenges was determined and given standard deviation. The outcomes are introduced in Table no-3

Friability

It is a proportion of mechanical strength of tablets. Roche friabilator was utilized to decide the friability by following method. Pre weighed capsules (20 tablets) were put in the friabilator. The tablets were turned at 25 rpm for 4 minutes (100 revolutions). Toward the finish of test, the tablets were re-gauged, misfortune in the heaviness of capsules is the proportion of friability and is communicated in Table no.3

\[
\% \text{ Friability} = \left[\frac{W1 - W2}{W1}\right] \times 100
\]
Where,
W1 = Initial weight of 20 tablets
W2 = Weight of the 20 tablets after testing

Table 3
Evaluation of Lozenges

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Potassium Curcuminate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight variation (mg)</td>
<td>2909±2.12</td>
</tr>
<tr>
<td>Thickness (mm)</td>
<td>4.23±0.04</td>
</tr>
<tr>
<td>Hardness (kg/cm²)</td>
<td>7.40±0.3</td>
</tr>
<tr>
<td>Friability (%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Content uniformity</td>
<td>94.21</td>
</tr>
</tbody>
</table>

*All information is offered in Mean ± SD, n=3, SD = standard deviation

**Preparation of standard solution**

Estimation of Potassium Curcuminate in 6.4 pH phosphate buffer. 100 mg of potassium curcuminate was dissolved in 100 ml of 6.4 pH phosphate buffer; the resulting solution was subsequently diluted with 6.4 pH phosphate buffer to obtain series of diluted concentrations i.e. 50, to 500 mcg/ml the absorbance of above diluted concentrations was measured at 464 nm using 6.4 pH buffer as blank. Estimation of potassium curcuminate in 6.4 pH phosphate buffer. 100 mg of potassium curcuminate was dissolved in 100 ml of 6.4 pH phosphate buffer; the resulting solution was subsequently diluted with 6.4 pH phosphate buffer to obtain series of diluted concentrations i.e. 50, to 350 mcg/ml the absorbance of above diluted concentrations was measured at 272 nm using 6.4 pH buffer as blank. Standard curve data reading are shown in table no.4

Table 4
Standard curve data for potassium curcuminate by UV-Visible spectrophotometer

<table>
<thead>
<tr>
<th>Serial No</th>
<th>Concentration in µg/ml</th>
<th>Average Absorbance (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>0.079±0.004</td>
</tr>
<tr>
<td>2</td>
<td>100</td>
<td>0.156±0.007</td>
</tr>
<tr>
<td>3</td>
<td>150</td>
<td>0.235±0.008</td>
</tr>
<tr>
<td>4</td>
<td>200</td>
<td>0.316±0.011</td>
</tr>
<tr>
<td>5</td>
<td>250</td>
<td>0.393±0.007</td>
</tr>
<tr>
<td>6</td>
<td>300</td>
<td>0.465±0.008</td>
</tr>
<tr>
<td>7</td>
<td>350</td>
<td>0.549±0.007</td>
</tr>
<tr>
<td>8</td>
<td>400</td>
<td>0.625±0.008</td>
</tr>
</tbody>
</table>
**Dissolution studies:**

In vitro dissolution studies for Potassium curcuminate. The vessel was filled with 200 ml phosphate buffer (6.4) and the Lozenges was placed in the inner perforated vessel. The metal bob was attached to the rod, the height of rod and bob was previously adjusted so that the bob completely touches the bottom of the perforated vessel. The apparatus was switched on and the bob was allowed to impact on the Lozenges. This process was continued for 2 hours. 5 ml sample of the buffer solution was withdrawn at a regular interval of 10 min and every time it was replaced with equal amount of phosphate buffer, thus the samples were collected at 10, 20, 30 upto 60 minutes. Results are shown in table-5

<table>
<thead>
<tr>
<th>Time in Minutes</th>
<th>Average Percent Drug Release</th>
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<tbody>
<tr>
<td>5</td>
<td>4.733±0.681</td>
</tr>
<tr>
<td>10</td>
<td>12.400±0.529</td>
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<tr>
<td>15</td>
<td>14.833±0.289</td>
</tr>
<tr>
<td>20</td>
<td>24.500±0.500</td>
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<td>25</td>
<td>36.000±1.000</td>
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<td>30</td>
<td>39.667±0.577</td>
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<tr>
<td>35</td>
<td>49.667±1.528</td>
</tr>
<tr>
<td>40</td>
<td>64.000±1.732</td>
</tr>
<tr>
<td>45</td>
<td>71.000±2.646</td>
</tr>
<tr>
<td>50</td>
<td>82.000±3.000</td>
</tr>
<tr>
<td>55</td>
<td>92.833±1.041</td>
</tr>
<tr>
<td>60</td>
<td>92.833±0.764</td>
</tr>
</tbody>
</table>

*All information is offered in Mean ± SD, n=3, SD = standard deviation*
Drug Release Kinetics

The mechanism of drug release from lozenges was determined by fitting the in vitro release profiles of optimized batches with zero order, first order, Hixson, Higuichi and Korsmeyer models. The obtained correlation coefficient values are given in the Table-6 & figure4-8.

Figure 3. Drug release from potassium curcuminate

Figure 4. Zero order model for drug release from potassium curcuminate lozenges

Figure 5. First order model for drug release from potassium curcuminate lozenges
Figure 6. Hixson Cromwell model for drug release from potassium curcuminate lozenges

Figure 7. Higuchi square root model for drug release from potassium curcuminate lozenges

Figure 8. Korsemeyer model for drug release from potassium curcuminate lozenges

Table 6
Comparative study of drug release from different models for potassium curcuminate lozenges

<table>
<thead>
<tr>
<th></th>
<th>ZERO</th>
<th>FIRST</th>
<th>HIGUCHI</th>
<th>HIXSON</th>
<th>KORSEMeyer</th>
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<tr>
<td>time</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>Observed</td>
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<tr>
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<td>% rel.</td>
<td>RS</td>
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<tr>
<td>0.05</td>
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<tr>
<td>0</td>
<td>33</td>
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<td>567</td>
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<tr>
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</tr>
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### Procedure for in vitro analysis of anti-cancer activity

The criteria for selection of a cell line for use in the interim panel were as follows.

- Adaptability to growth on a single medium (RPMI-1640 plus 5% fetal bovine serum and 2mM glutamine):
- A negative test for mycoplasma and mouse antibody production.
- Isoenzyme and karyotype profiles verifying the human origin of cells.
- Mass doubling that allows for harnessing of approximately 3x10^7 cells twice a week: and
- Suitability for use with microculture assays.

Once a line had been established as suitable, the number of cells was massively expanded in minimal number of passages and the cells were cryopreserved in a large repository of ampoules each containing 1x10^6 cells to provide a consistent frozen stock for future use. Once the growth in the in the new stock is established at the second or third passage, the older passage line is replaced with the new.
stock established at the second or third passage, the older passage line is replaced with the new stock for use in the screening laboratory.

**Cell line maintenance**

Cells are maintained in multiple of T150 tissue culture flasks. Cells for each inoculation day are maintained separately (no common reagents) and passaged on separate days to prevent catastrophic loss of growing cell line stocks to microbial contamination. Additional backup flasks of cells are also maintained. For each cell line, the seeding density per flask is determined for production of healthy culture of 70% to 90% after 7 days for continued routine maintenance. These seeding densities than utilized twice a week to maintain sufficient cells for anti-cancer drug screening.

**Preparation and inoculation of cells**

All of the adherent cell lines are detached from the culture flasks by addition of 2-3 ml of 0.05% trypsin-EDTA. Thereafter trypsin is inactivated by addition of 10 ml of 5% serum containing RPMI 1640 medium. Cells are separated into single cell suspension by gentle pipetting action then counted using trypan blue exclusion on a hemacytometer or by Coulter counter which is used when viability as determined by trypan- blue exclusion routinely greater than 97%. After counting dilutions were made to give the appropriate cell densities for inoculation onto the micrometer plate. Cells were inoculated in a volume of 100μl per well at densities between 5000 and 40000 cells per well. Cells were counted diluted and inoculated onto microculture plates within 4 hours period on 2 days each week. The micrometer plates containing the cells are preincubated for approximately 24 hours at 370C to allow stabilization prior to addition of drug.

**Solubilization and dilution of samples**

For the initial screening of pure compounds each agent is routinely tested at five 10 fold dilutions starting from a maximum concentration of 104 M. Alternatively a maximum of 10 M can be selected if solubility permits. All samples are initially solubilized in dimethyl sulfoxide (DMSO) or water at 400 times the desired final maximum test concentration. Drug stocks are not filtered or sterilized, but microbial contamination is controlled by addition of gentamicin to the drug diluent. Multiple aliquots are stored at frozen at -700C to provide uniform samples for initial for tests as well as retests, if required just prior to preparation of the drug dilutions in cell-culture medium. These frozen concentrates are thawed at room temperature for 5 minutes. The concentrates are then diluted with complete medium containing 50 μg/ml gentamicin to twice the desire final concentrations.

**Drug incubation**

Immediately after preparation of these intermediate dilutions 100μL aliquots of each dilution were added to the appropriate microtiter plate wells according to the format. As the microtiter wells already contain the cells in 100μL of medium, the final drug concentration tested is 50% of that in the intermediate dilutions.
Agents are then added immediately to the cultures in the microtiter plates. During development of these procedures, drug incubation time was 1, 2, 3, 4 or 6 days at 37 °C in an atmosphere of 5% CO2 and 100% relative humidity. The plates were been assayed for the cellular growth and viability by microculture assay by tetrazolium assay or by SRB assay. In the current screening procedure, the cultures were incubated with test agents for 2 days and the end point is measured by the SRB assay.

Microculture tetrazolium assay. The MTT assay is based on metabolic reduction of 3-(4, 5- dimethyl thiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT). A 50μl aliquot of MTT solution (1mg/ml) in RPMI-1640 medium, with no serum or glutamine, is added directly to all the appropriate microtiter plate wells containing cells complete growth medium and test agents. The culture is then incubated for 4 hrs to allow for MTT metabolism to formazan. After this time the supernatant is aspirated and 150μl of Dimethyl sulfoxide is added to dissolve the formazan. Plates are agitated on plate shaker to ensure a homogenous solution, and the optical densities are read on an automated spectrophotometric plate reader.

Sulforhodamine bio assay: Adherent cell cultures were fixed in situ by adding 50 μl of cold 50 % (wt/vol) trichloroacetic acid (TCA) and incubating for 60 minutes at 40°C. The supernatant is then discarded and the plates were washed five times with deionized water and dried. One hundred microliters of SRB solution (0.4% wt/vol in acetic acid) is added to each microtiter well and the culture is incubated for 10 minutes at room temperature. Unbound SRB is removed by washing five times with 1 % acetic acid. Then the plates are air dried. Bound stain is solubilized with Tris buffer and the optical densities are read.

Data Calculations

Unprocessed optical density data from each microtiter plate are automatically transferred from the plate reader to a microcomputer, where the background optical density (OD) measurements (i.e. complete medium plus stain minus cells) are subtracted from the appropriate control well values and where the appropriate drug- blank measurements (i.e. complete medium plus test compound dilution plus stain, minus cells) are subtracted from appropriate test well values. The values for mean + SD of data from replicate wells were calculated. Data are expressed in terms of % T/C [(OD of treated cells/ OD of control cells) x 100] as measure of cells viability and survival in the presence of test materials. Calculations are also made for the concentration of test agents giving a T/C value of 50% or 50% growth inhibition (IC50) and a T/C value of 10% or 90% growth inhibition (IC90).

With the SRB assay, a measure is also made of the cells population density at time (the time at which drugs are added) from two extra reference plates of inoculated cells fixed with TCA just prior to drug addition to the test plates. Thus we have three measurements controls optical density (C), test optical density (T) and optical density at tie zero (T0). Using these measurements, cellular responses can be calculated for growth stimulations for no drug effect and for growth inhibition. If T is greater than or equal to T0, the calculation is 100x [(T-T0)/(C-T0)]. If T is less than T0, cell killing has occurred and can be calculated from 100x
\[
\frac{(T-T_0)}{T_0} \text{. Growth inhibition of 50% (GI50) was calculated from } 100 \times \frac{(T-T_0)}{C-T_0} = 50, \text{ which is the drug concentration causing a 50% reduction in the net protein increase in control cells during the drug incubation. The drug concentration resulting in total growth inhibition (TGI) was calculated from } T = T_0. \text{ Where the amount of protein at the end of drug incubation is equal to the amount of protein at the end of drug incubation is equal to the amount at the beginning. The final calculation, LC50, is the concentration of drug causing a 50% reduction in the measured protein at the end of the drug incubation, compared with that at the beginning. Indicating a net loss of cells following drug treatment. LC50 is calculated from } 100 \times \frac{(T-T_0)}{T_0} = -50. \text{ Results are shown in table no. 7.}
\]

<table>
<thead>
<tr>
<th>Name of Drug</th>
<th>Conc. (µg/ml)</th>
<th>PC-3 Prostate</th>
<th>HEP-2 Liver</th>
<th>A-549 Lung</th>
<th>502713 Colon</th>
<th>HCT-15</th>
<th>SW-620</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green tea extract</td>
<td>100</td>
<td>46%</td>
<td>4%</td>
<td>28%</td>
<td>94%</td>
<td>83%</td>
<td>9%</td>
</tr>
<tr>
<td>Potassium curcuminate</td>
<td>100</td>
<td>85%</td>
<td>80%</td>
<td>52%</td>
<td>92%</td>
<td>89%</td>
<td>95%</td>
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<td>Curcumin</td>
<td>100</td>
<td>58%</td>
<td>32%</td>
<td>36%</td>
<td>74%</td>
<td>82%</td>
<td>51%</td>
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<td>5-Fu</td>
<td>1x10-4M</td>
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<td>24%</td>
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<td>65%</td>
<td>44%</td>
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<td>69%</td>
<td>24%</td>
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<td>66%</td>
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<td>Paclitaxel</td>
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<td>26%</td>
<td>-</td>
<td>37%</td>
<td>71%</td>
<td>73%</td>
<td>-</td>
</tr>
</tbody>
</table>

**Results**

Potassium curcuminate exhibits targeted anticancer effect against Prostate, Liver, Lungs and colon cancer cell line. Anticancer effect of potassium curcuminate was estimated by MTT assay and morphological studies. The results of the MTT assay, Sulforhodamine bio assay revealed wide anticancer activity of the potassium curcuminate towards Prostate, Liver, Lungs and Colon cancer cells. Potassium curcuminate greatest anticancer activity 85% towards prostate cancer cell, 80% towards liver cancer cell, and average of 92% towards colon cancer cell compared to curcumin and standard anticancer drugs like 5-Fu, Mito-C and Paclitaxel.

**Conclusion**

Lozenges show many benefits over the other dose type of these are; direct simple to geriatric and pediatric populace, has great taste, it draws out the time of medication in the oral cavity to deliver a particular impact, arranged effectively and no need water consumption for organization, this study planned to form potassium curcuminate as lozenges to further develop conveyance to treat oral thrush. The pre-arranged definitions were exposed to different physical and Chemical tests like assay, weight variation invitro drug release. Finally it was
concluded that the potassium salt of Curcumin lozenges can be considered as a suitable delivery system for the treatment variety of Cancer.

References

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