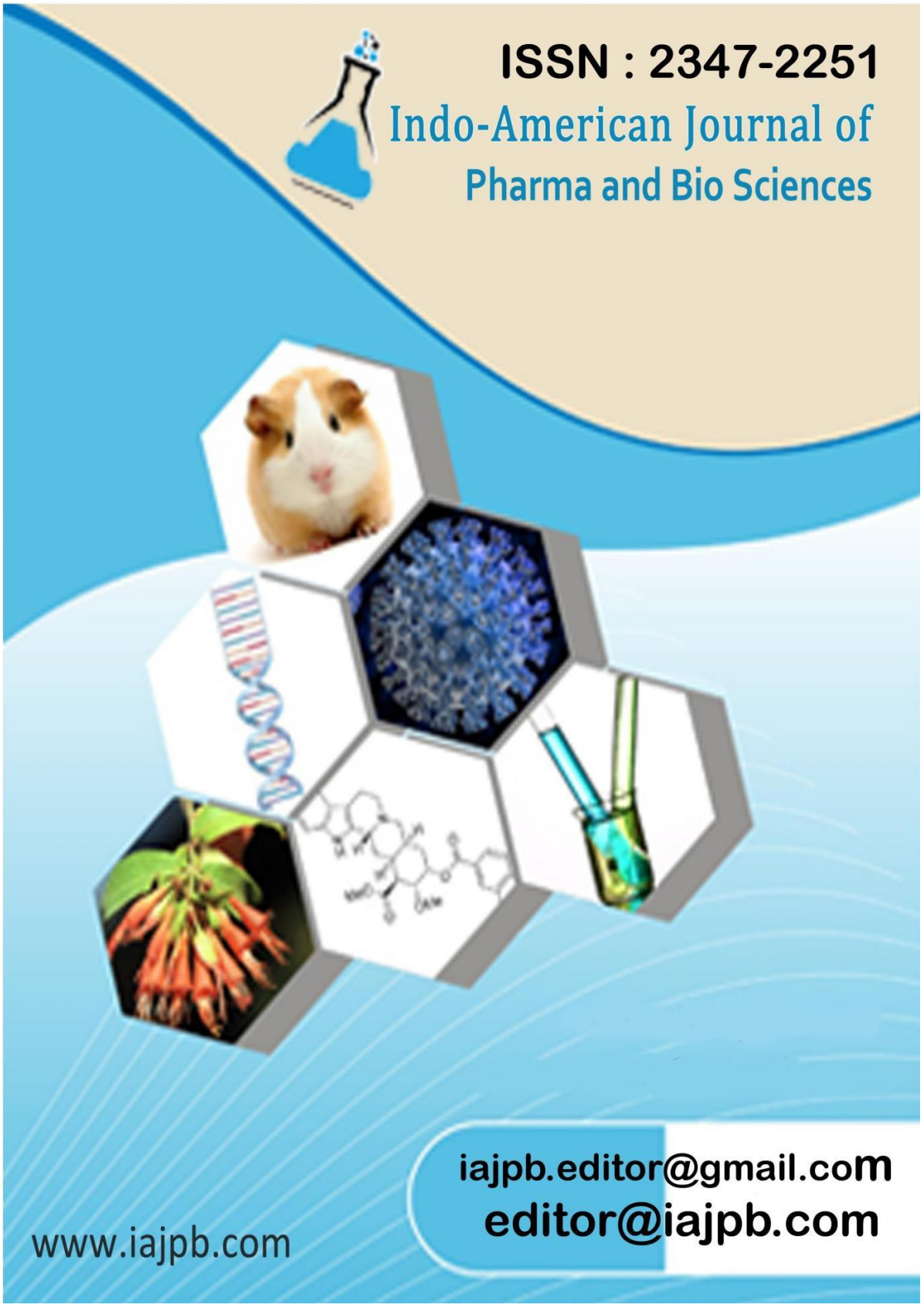

ISSN : 2347-2251
Indo-American Journal of
Pharma and Bio Sciences
iajpb.editor@gmail.com
editor@iajpb.com
www.iajpb.com

Indo-Am. J. Pharm & Bio. Sc., 2023 *ISSN 2347-2251 www.iajpb.com*

Indo-American Journal of Pharma and Bio Sciences

Vol. 20, Issuse 4, Nov 2022

FORMULATION AND EVALUATION OF CONTROLLED RELEASE VITAMIN "C" MICROPARTICLES

Dasari Ramya R.Mohanthi , K.Venkat Krishna Dr. G. ChinnaDevi .,

Article Info

Received: 19-08-2022 Revised:10 -09-2022 Accepted: 02-10-2022

ABSTRACT

With the use of cellulose polymers such hydroxypropyl methyl cellulose, cellulose acetate phthalate, and ethyl cellulose, the current work aims to produce vitamin C microparticles. Microparticles were produced utilising the Emulsion Solvent Evaporation Technique. To evaluate the physicochemical characteristics of vitamin C microparticles, techniques such as FTIR, frequency distribution analysis, percent drug entrapment efficiency, in vitro drug release, and release kinetics were applied. The FTIR spectrum showed that polymers and pure medicines could coexist. It was possible to obtain the typical frequency distribution of the vitamin "C" microparticles. Maximum drug entrapment effectiveness was attained in Vitamin "C" Microparticles at 98.7%. The performance of vitamin "C" microparticles in a test tube showed that the concentration of polymers affected control release. Regression coefficient values indicate that the data were published with an order of 0. According to the study, the polymers used had an effect on how much Vitamin "C" was released from the small particles. It was shown that the used cellulose derivatives restricted the medication release. Among the cellulose derivatives tested, ethyl cellulose microparticles with a core:coat ratio of 1:1 were shown to have a better controlled release of vitamin "C" over a period of 12 hours.

KEY WORDS: Vitamin 'C', Cellulose polymers, Microencapsulation

INTRODUCTION

Microencapsulation is the process of completely enclosing a substance in a thin layer or embedding it in a very tiny quantity of homogeneous or heterogeneous matrix.

Microencapsulation of biomolecules is a sophisticated method used by the pharmaceutical industry in search of innovative materials that improve the drug's stability and release state.

Solvent evaporation microencapsulation is often used because it permits the controlled release of a drug. The best polymers for encapsulating are those that cannot be dissolved in water.

Vitamin C is also known as ascorbic acid. Because of its antioxidant properties, this polymer may be dissolved in water. Vitamin C may be helpful for your bones, connective tissues, muscles, and blood vessels. Ascorbic acid may help stop vitamin C deficiency.

Department of pharmaceutics,
Department of pharmaceutics
Department of pharmaceutics,
industrial pharmaceutics

University College of Pharmaceutical Sciences, Mahabubnagar Telangana state-509001.
Mail id: dasariramyapatel@gmail.com

Encapsulating provides additional safety by covering active molecules with secondary compounds. The capsule provides excellent protection for the active ingredient by isolating it from the ambient environment. This transformation, through which the volatile active molecules are converted into

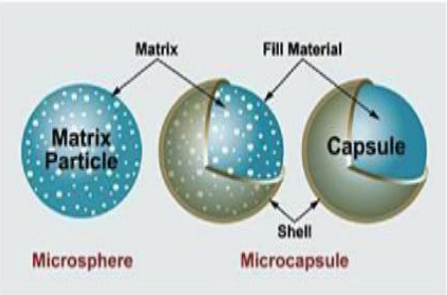


Figure 1 Structure of micro particle

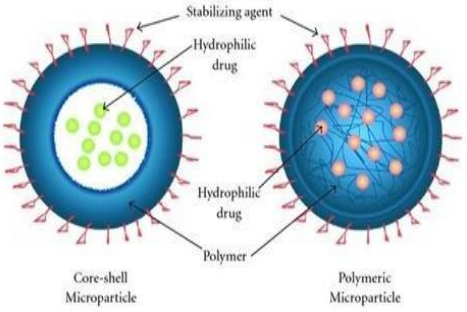


Figure 2 Schematic view of Micro particle

SALIENT FEATURES OF MICROSPHERES

- This technique is useful for masking disagreeable flavours and reducing the viscosity of oil and other liquids.
- Drug protection against the elements
- One of the major functions of buffers is to avoid incompatibilities between the medication and its intended receivers, while another is to slow the pace at which a drug loses its volatile qualities.
- Dispersion of water-insoluble substances in aqueous media; production of sustained-release, controlled-release, and target-specific medications; improvement of flow characteristics; safe management of taste masking;

DRUG PROFILE[43, 44,45]

Drug Name : Vitamin "C"

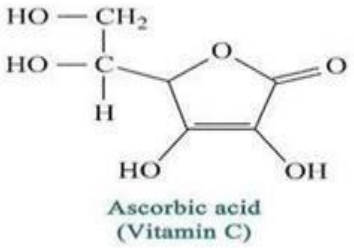
IUPAC Name : (5R)-[(1S)-1,2-Dihydroxyethyl]-3,4-dihydroxyfuran-2(5H)-one

Synonyms : L-ascorbic acid, Ascorbic acid

Description

Several critical processes rely on vitamin C, also called ascorbic acid. In this way, vitamin C serves as an antioxidant. This includes doing things like shielding cells and maintaining their health. Keeping your skin, blood vessels, bones, and cartilage in tip-top shape. facilitating the healing of wounds.

Structure



Ascorbic acid
(Vitamin C)

Molecular formula: $C_6H_8O_6$

Molecular weight: 176.12 g/mol

PHYSICAL PROPERTIES

State : Solid

Colour : White colour

Odour : Acidic scent

Melting point : 190–192°C

Solubility : Water (300 g/L at 20°C)

Density : $1.65 g/cm^3$

Pharmacodynamics

For example, vitamin C in the form of acerbate acts as an enzyme substrate or cofactor and an electron donor, among many other roles, in the human body.

Pharmacokinetics:

It is true that vitamin C's pharmacokinetics are difficult to understand. Absorption and elimination are principally controlled by a class of reversible sodium dependent transporters (SVCTs), which are dose-dependent.

Bioavailability	:	70%-90%
Protein binding	:	25%
Half-life	:	10–12 hours
Dose	:	70-120 mg/day
Category	:	Anti-Oxidant

Metabolism

Hepatic. Dehydroascorbic acid is formed when hydrogen is removed from the ascorbic acid remedial group, an oxidation process that may be reversed. It is physiologically active in two forms present in bodily fluids. Oxalic acid and ascorbyl-2-sulfate, both inert molecules, are produced from ascorbic acid during metabolism.

Medicinal uses

- Scurvy
- Infection
- COVID-19
- Cancer
- Cardiovascular diseases
- Brain functions
- Iron deficiency

Adverse Effects

- Nausea
- vomiting
- Heartburn
- Stomach cramps or bloating
- Fatigue
- Insomnia
- Headache

2. MATERIALS AND METHOD

Chemicals and reagents: The following ingredients were purchased from Spansules Pharmatech pvt, ltd. in Hyderabad, India: vitamin C; ethyl cellulose; cellulose acetate phthalate; hydroxypropyl methyl cellulose; ether; chloroform; ethanol; light liquid paraffin; tween 80; methanol; methylene dichloride; hydrochloric acid.

Preparation of Microparticles:

The solvent was evaporated from an emulsion to form microparticles of vitamin 'C' with a controlled release. Intense magnetic stirring is applied to an organic phase including drug ethyl cellulose dissolved in chloroform, cellophane acetate phthalate dissolved in ether, and hydroxypropyl methyl cellulose dissolved in ethanol and methylene dichloride in various amounts (1000rpm, 5min). After waiting around five minutes, 160 ml of light liquid paraffin and PVA containing tween 80 (0.4%) were syringe-emulsified from the organic phase.

The emulsion was mixed for three hours at room temperature using a mechanical stirrer equipped with a propeller with three blades. After being filtered out, microparticles were washed three times in n-hexane and dried in a vacuum dehydrator. desiccator at room temperature for 48 hrs.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Vitamin C (mg)	75	75	75	75	75	75	75	75	75
Ethyl Cellulose (mg)	37.5	75	150	-	-	-	-	-	-
Cellulose acetate phthalate(mg)	-	-	-	37.5	75	150	-	-	-
Hydroxy propyl methyl cellulose(mg)	-	-	-	-	-	-	37.5	75	150
Chloroform(ml)	30	30	30	-	-	-	-	-	-
Ether (ml)	-	-	-	30	30	30	-	-	-
Ethanol and Methylene dichloride(ml)	-	-	-	-	-	-	30	30	30
Liquid paraffin(ml)	160	160	160	160	160	160	-	-	-
Tween 80(ml)	0.64	0.64	0.64	0.64	0.64	0.64	-	-	-
Poly vinyl alcohol(ml)	-	-	-	-	-	-	500	500	500

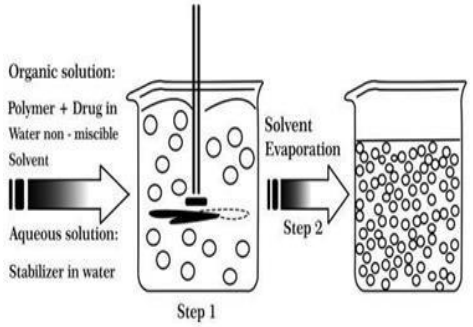


Figure 3: Preparation of Micro particles

EVALATION:

1. Preparation of Standard Calibration Curve:

Vitamin ‘C’:Dilution Medium (1:1)

Methanol Distilled waterPrinciple:

Vitamin C has an absorbance peak at 243nm and is soluble in methanol.

Standard solution of Vitamin „C‟:

For the first stock solution-I, 100 mg of vitamin 'C' was dissolved in a dilution medium to achieve a concentration of 1000 g/ml.

A second stock solution (II) was made by dissolving 10 millilitres of the first stock solution (I) into 100 millilitres of a methanol and water dilution medium. The resulting solution had a concentration of 100 micrograms per millilitre.

Aliquots of standard drug solution (0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml, and 1 ml) were drawn from stock solution-II and poured into 10 ml volumetric flasks, where they were diluted to the appropriate concentrations (2, 4, 6, 8, and 10 g/ml, respectively). The UV-spectrophotometer was used to compare the maximum absorbance of each solution to that of a blank made up of dilution media at 243 nm. A chart was drawn using concentration vs absorbance.

2. ORGANOLEPTIC PROPERTIES

Colour and nature

A white sheet of paper was used to spread out a little amount of the sample powder for visual inspection.

Taste and odour

Vitamin 'C' was employed primarily for olfactory (through the nose) and gustatory (through the tongue) perceptions of taste.

PHYSICAL CHARACTERISTICS

Bulk density

- Density in bulk is defined as the mass per unit volume of a powder. primarily bulk density.
- There is an increase in bulk density as the particle approaches a spherical form.
- Bulk density is calculated by weighing a given quantity of powder and then measuring the volume of the powder after it has been sieved into a graduated cylinder.

Procedure

Powder of a known mass was placed into a measuring cylinder, and the cylinder was carefully levelled without compacting the powder. To get the bulk density in grammes per millilitre, use the following formula.

$$D_b = M/V_b$$

Where,

D_b = Bulk density

M = Mass of powder.

V_b = Bulk volume of the powder.

Tapped density

The tapped density of a powder is defined as the mass per unit volume after being tapped.

Procedure

A funnel was held at a certain height above a piece of paper spread out on a tabletop by means of a vertical support. After closing the funnel's bottom, 10g of powdered sample is added. Angles of repose may be determined using the following expression.

Angle of repose (θ) = $\tan^{-1}(h / r)$

Where,

h = height of the powder piler = radius of pile circle

Table 4: Angle of Repose Limits

ANGLE OF REPOSE	FLOWABILITY
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Hausner‟s ratio:

The Hausner ratio is a proxy for the fluidity of powder. Using this formula, we were able to determine it.

$$\text{Hausner's ratio} = \frac{\text{Tapped Density}}{\text{Bulk density}}$$

Table5: Hausner"s Ratio values

Hausner's ratio	Type of flow
<1.25	Good
1.25-1.5	Moderate
>1.5	Poor

Carr"s index (I):

It is a measure of the powder's granularity and flowability. It's a percentage that's calculated by,

$$C.I = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped density}} \times 100$$

Table 6: Carr"s index values

Carr's index (%)	Type of flow
5-15	Excellent
12-18	Good
12-23	Fair to passable
23-35	Poor
35-38	Very poor
>40	Extremely poor

C) Melting point determination:

The melting point is the temperature at which a pure liquid and solid are both present. In common use, it is assumed that the mixture is in equilibrium at an external pressure of 1 atmosphere, leading to the term "normal melting points."

3. Percentage yield of micro particles:

All batches of ready-to-use microparticles had their weights confirmed to within a margin of error. Total percentage yield of microspheres was calculated by dividing the weight quantity of produced micro particles by the sum of all receivers and drug employed in microsphere manufacturing. The following equation was used to get this value:

$$\%\text{yield} = \frac{\text{Actual weight of product}}{\text{Total weight of excipient and drug}} \times 100$$

4. Particle size analysis:

The particles' size distribution was analysed by sifting them using a series of typical BSS sieves. Furthermore, mean number weighted size was determined by optical microscopy utilising a stage micrometre slide and a calibrated eyepiece. More than 100 tiny particles had their sizes randomly tested under the microscope.

$$\text{dmean} = \frac{\sum nd}{\sum n}$$

5. Drug entrapment

The total number of microspheres containing the medication is determined based on the 100mg dosage. This quantity sterilization-mixed with 0.1 N HCL. Pipette 1 ml from there into a 10 ml volumetric flask, and then fill the rest of the way with buffer. After proper dilution, spectrophotometric absorbance at 243 nm was measured in comparison to a blank solution. The following calculations were used to determine the total quantity of medication contained inside the microspheres.

$$\%\text{DEE} = \frac{\text{Amount of actually drug present}}{\text{Theortical drug loaded excepted}} \times 100$$

6. Drug content of the Micro particles:

Extraction of medicines from microparticles allowed us to spectrophotometrically measure the loading efficiency of vitamin C. This was done at the maximum wavelength of 243 nm. Five milligrammes of microparticles were crushed and then vortex-mixed with ten minutes' worth of ether. The extract was then poured into a 50 mL volumetric flask and the capacity was completed with ether. In order to determine the concentration, a UV visible spectrophotometer was used at 243 nm with a blank of the suitable wavelength. The microspheres' drug content was determined.

7. INVITRO DISSOLUTION STUDIES

Preparation of 0.1 N HCl:

In a 1000 ml volumetric flask, add 8.5 ml of concentrated hydrochloric acid and fill the rest

of the way with distilled water; swirl to combine.

In-vitro release profile:

Medium : 0.1 N HCL

Apparatus : USP II (Paddle)

Speed : 100 rpm

Time : 12hr

Temperature: 37.5°C

λ max : 243 nm

Microspheres should be tested in 0.1N HCL at 37 °C 0.5 °C, and each dissolving vessel should contain 900 ml of the solution. To determine the percentage of release, a sample was obtained at the designated time and then replaced with the same volume of 0.1 N Hcl to keep the sink conditions constant before measuring absorbance. Each product was tested three times, and the average and standard deviation were tallied. The percentage of drug release was then plotted as a function of time to examine the drug's release pattern.

8. KINETIC RELEASE STUDY Zero-order model

Drug dissolution from It is possible to model the delayed release of a medication from a non-disaggregating dosage form using the equation:

$$Q_0 ñ Q_t = K_0 t$$

Rearrangement of equation

$$Q_t = Q_0 + K_0 t$$

K0 is the zero order release constant, given as a concentration per unit time, and Qt is the amount of drug dissolved at time t. Q0 is the initial concentration of drug in the solution (usually Q0 = 0).

Results from in vitro drug release studies were shown as the cumulative amount of drug released over time to examine the release kinetics.

In the pharmaceutical business, this correlation may be used to describe the dissolution of a broad range of transversal systems, matrix tablets containing low soluble drugs in coated forms, osmotic systems, etc.

Table 8: Mechanism of drug release

S. No	n values	Drug release
1	0-0.5	Fickian release
2	0.5-1.0	Non-Fickian release
3	>1.0	Class II transport

3. RESULTS AND DISCUSSION

STANDARD CALIBRATION CURVE FOR VITAMIN "C"

Vitamin C Calibration Curve Vitamin C's spectroscopic ally determined wavelength in methanol is 243 nm. The acquired drug sample was pure, as shown by the linear relationship between absorbance and concentration in the range of 0–10 g/ml, which is in accordance with IP standards.

Table 9: Standard curve of Vitamin „C"

Concentration(µg/ml)	Absorbance
0	0
2	0.218
4	0.4076
6	0.5923
8	0.79
10	0.959

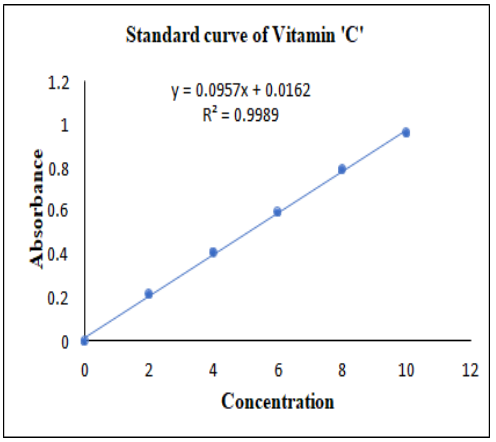


Figure 4: Standard Curve of Vitamin 'C'

DRUG POLYMER INTERACTION STUDY: FTIR STUDIES

Discussion

Vitamin C polymerization is predicted by the vitamin C spectrum. The drug and polymer IR

spectra demonstrate that all typical peaks of Vitamin C were present in the combined spectrum.

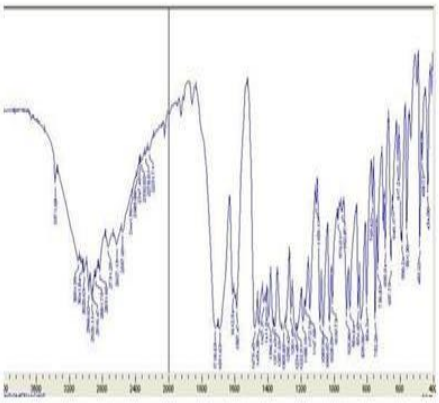


Figure 5: FTIR spectra of Vitamin 'C'

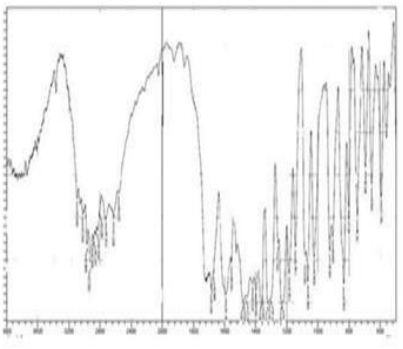


Figure 6: FTIR spectra of physical mixture of Vitamin 'C' and HPMC

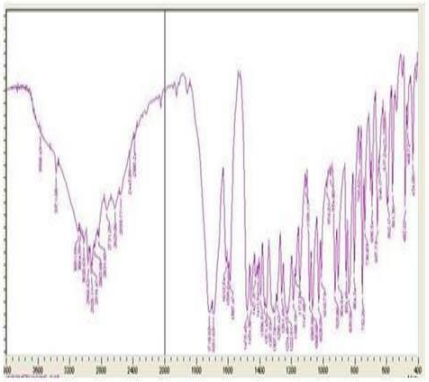


Figure 7: FTIR spectra of physical mixture of Vitamin 'C' and CAP

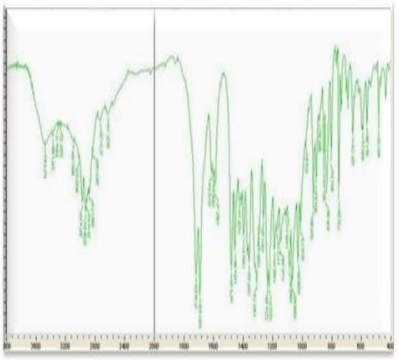


Figure 8: FTIR spectra of physical mixture of Vitamin 'C' and ECDiscussion

The IR value of pure drug was C=O: 1718.63,-O-:1290.42CH3:2658.13, -COOH: 3371.68,

The IR values of pure drug and polymer (EC) was =O: 1718.63, -O-

: 1290.43, NO2:1479.45, -CH3:2627.13, -COOH: 3371.68, -Cl: 752.26],

The IR values of pure drug and polymer (CAP) were [C=O: 1718.63, -O-

: 1290.43, NO2:1479.45, -CH3:2658.06, -COOH: 3371.68, -Cl: 752.45,

-COOR: 2380.3],

The IR values of pure drug and polymer (HPMC) was [C=O: 1681.98, - O-1301.0, NO2:1484.63,-CH3:2627.13, -Cl: 747.44].

The FTIR spectrum shows that the polymers and the pure medication may coexist safely.

PRE FORMULATION STUDIES

Taste and smell are called organoleptic qualities.

These analyses were carried out in accordance with the prescribed process, namely the Preformulation phase. The findings are shown in the table below.

Table 10: Organoleptic properties

Test	Specifications/limits	Observations
Colour	White to off white	White powder
Odour	Odourless	Odourless
Taste	Tart flavour	Tart flavour

The outcomes are in line with expectations.

Aspects of Nature

Bulk density and tapped density

It was calculated using the approach described in the Preformulation section of the materials and methods. The outcomes are shown in the table below.

Table 11: Density

Materials	Bulk Density (gm/ml)	Tapped density (gm/ml)
Vitamin 'C'	0.5	0.57

Angle of repose

Preformulation approach in the materials and methods section was used to get this conclusion. A table depicting the findings is provided below.

Table 12: Flow properties

Material	Angle of repose
Vitamin 'C'	29°.28"

The result shows that drug having good flow

Melting point

It was calculated using the approach described in the Preformulation section of the article on materials and methods. A table depicting the findings is provided below.

Table 13: Melting point

Material	Melting point range	Result
Vitamin 'C'	190°C-192°C	190°C

Research on Vitamin C's Angle of Repose, Bulk Density, and Tapped Density was conducted in advance of its commercialization, and the data were collated according to IP requirements. Having a melting temperature of 190 degrees Celsius, Vitamin C was determined to be pure enough to meet IP criteria.

EVALUATION OF MICROPARTICLES

Particle Size Determination

Table 13: Average particle size of Vitamin „C" Microparticles

Formulation	Average size(µm)±SD
F1	412±3.13
F2	448±4.10
F3	453±5.18
F4	519±2.13
F5	524±4.12
F6	553±1.25
F7	601±1.01
F8	625±1.18
F9	651±3.21

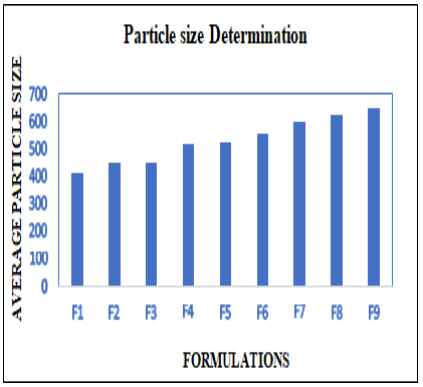


Figure 9: Partical Sizeof Vitamin C Microparticles

Discussion:

Increasing the polymer content led to a considerable rise in the mean particle size of the vitamin C micro particles, placing them within the range required for formulation. F1 to F3 is 412±3.13 to 453±5.18, F4 to F6 is 519±2.13 to 553±1.25, F7 to F9 is 601±1.01 to 652±3.2µm.

Percentage Yield, % Drug Content Drug Entrapment Efficiency

Determination

Table 14: Values of Percentage yield, % Drug content, % DEE

Formulation	Percentage Yield (%)	Drug Content (%)	DEE (%)
F1	57.18	42.7	90
F2	84.65	37.8	91.52
F3	88.01	34.2	98.6
F4	93.55	25.76	98.5
F5	93.91	23.38	98.5
F6	93.48	21.3	98.7
F7	81.40	33.0	94.28
F8	84.60	27.96	94.40
F9	76.80	22.58	95.70

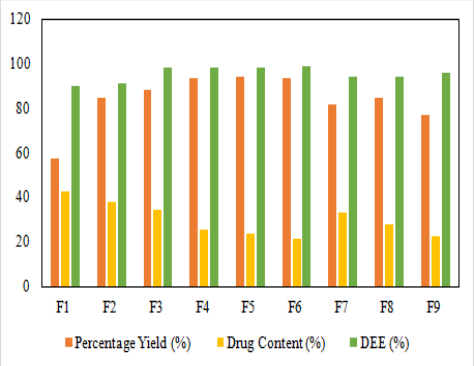


Figure 10: Drug Entrapment Efficiency of Vitamin 'C' Microparticles

Discussion

Three polymers—Ethyl cellulose, Cellulose Acetate Phthalate, and Hydroxy propyl Methyl Cellulose—were utilised to create the microspheres that were then tested for their effects on encapsulation efficiency.

F5 formulation was determined to have the highest yield of all formulations, at 93.91%. F1 was tested and determined to have a drug content of 42.7% and %. F6 had the highest drug entrapment efficiency of all of the formulations tested, at 98.7 percent.

INVITRO DISSOLUTION STUDIES

Table 15: In-vitro dissolution studies of formulation of F1-F5

Time (Min)	F1	F2	F3	F4	F5
	%CDR±SD	%CDR±SD	%CDR±SD	%CDR±SD	%CDR±SD
15	3.07±1.62	3.00±0.61	2.10±1.06	3.13±0.59	2.06±0.23
30	5.80±1.06	5.06±0.61	4.14±0.61	5.01±0.59	4.60±0.23
60	9.70±1.06	8.05±0.61	6.98±1.06	7.78±0.59	6.95±0.23
120	19.80±1.23	15.67±0.61	12.18±0.00	14.44±0.59	12.82±0.23
180	29.45±2.21	22.57±1.06	18.73±0.61	21.36±0.59	18.84±0.63
240	40.65±1.62	29.13±0.61	24.93±0.61	30.80±1.03	25.62±0.00
300	50.60±2.21	39.10±1.06	33.78±1.06	36.22±0.59	31.09±0.23
360	63.70±1.62	47.66±0.61	42.33±1.22	44.33±0.59	37.42±0.63
480	82.00±1.23	64.34±1.06	56.80±1.06	58.51±1.58	51.80±0.41
600	96.07±1.23	80.07±1.06	70.70±0.61	69.76±2.09	59.06±0.41
720		96.87±1.04	82.80±1.22	80.45±1.58	68.09±0.23

Table 16: Invitro dissolution studies of Formulations F6-F9

Time (min)	F6	F7	F8	F9	Marketed
	% CDR±SD	% CDR±SD	% CDR±SD	% CDR±SD	% CDR±SD
15	2.55±0.31	3.65±0.11	2.75±0.23	2.05±0.59	11.3±1.06
30	3.94±0.20	6.46±0.11	4.77±0.23	4.11±0.59	21.34±1.24
60	4.90±0.41	8.89±0.20	6.84±0.41	6.07±0.79	30.1±0.61
120	10.30±0.54	17.97±0.41	13.97±0.24	11.90±0.30	36.11±0.65
180	15.72±0.20	27.46±0.31	21.69±0.41	17.26±0.51	43.13±1.01
240	20.53±0.12	36.22±0.35	28.99±0.86	23.46±0.51	51.2±1.00
300	25.60±0.23	47.45±0.23	36.84±0.72	30.96±0.59	65.42±2.44
360	30.89±0.23	59.62±0.11	43.83±1.09	36.29±1.37	78.12±3.04
480	36.78±0.11	78.58±0.31	56.13±1.92	49.61±1.79	84.2±1.33
600	44.01±0.23	96.28±0.63	68.04±1.20	61.06±1.67	98.02+1.01
720	48.05±0.20	_	83.67±0.45	74.08±1.69	

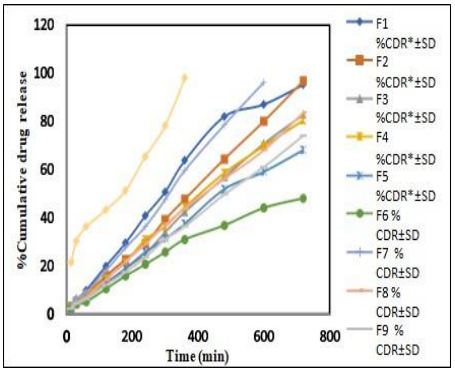


FIGURE: 11 INVITRO RELEASE OF VITAMIN C MICTROPARATICLES

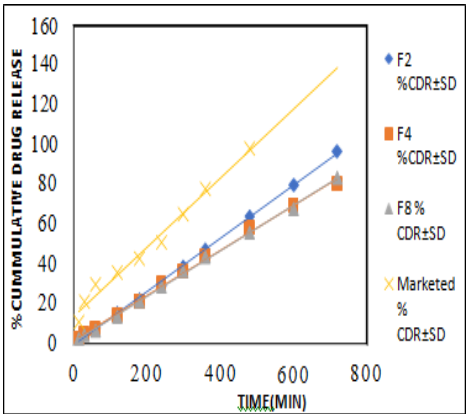


Figure 12: Comparative in vitro dissolution of Vitamin C MicroparticlesWith marketed product

RELEASE KINETICS

presents a graphical depiction of the in vitro vitamin C microparticle release kinetics for formulations F1 through F9. We modelled drug release from Vitamin C Micro particles using the Higuchi square root of time and Korsemeyer-Peppas equations, and we found that they fit our data the best.

A fit of the Korsmeyer-Peppas equation to the release data provides more evidence in favour of a diffusion-controlled mechanism. Non-Fickian diffusion was shown to control the movement of vitamin C microparticles across a wide range of exponent 'n' values (-100 to +100). 0.5 and 1.

Table 17: Zero order release kinetic data of Vitamin C Micro particles of F1-F5

Time (min.)	%Cumulative drug release				
	F1±SD	F2±SD	F3±SD	F4±SD	F5±SD
15	3.07±1.62	3.00±0.61	2.10±1.06	3.13±0.59	2.06±0.23
30	5.80±1.06	5.06±0.61	4.14±0.61	5.01±0.59	4.60±0.23
60	9.70±1.06	8.05±0.61	6.98±1.06	7.78±0.59	6.95±0.23
120	19.80±1.23	15.67±0.61	12.18±0.00	14.44±0.59	12.82±0.23
180	29.45±2.21	22.57±1.06	18.73±0.61	21.36±0.59	18.84±0.63
240	40.65±1.62	29.13±0.61	24.93±0.61	30.80±1.03	25.62±0.00
300	50.60±2.21	39.10±1.06	33.78±1.06	36.22±0.59	31.09±0.23
360	63.70±1.62	47.66±0.61	42.33±1.22	44.33±0.59	37.42±0.63
480	82.00±1.23	64.34±1.06	56.80±1.06	58.51±1.58	51.80±0.41
600	96.07±1.23	80.07±1.06	70.70±0.61	69.76±2.09	59.06±0.41
720	-	96.87±1.04	82.80±1.22	80.45±1.58	68.09±0.23

Table 18: Zero order release kinetic data of Vitamin C Microparticles of F6-F9 &Marketed product

Time (min.)	%Cumulative drug release				
	F6±SD	F7±SD	F8±SD	F9±SD	Marketed
15	2.55±0.31	3.65±0.11	2.75±0.23	2.05±0.59	11.3±1.06
30	3.94±0.20	6.46±0.11	4.77±0.23	4.11±0.59	21.34±1.24
60	4.90±0.41	8.89±0.20	6.84±0.41	6.07±0.79	30.1±0.61
120	10.30±0.54	17.97±0.41	13.97±0.24	11.90±0.30	36.11±0.65
180	15.72±0.20	27.46±0.31	21.69±0.41	17.26±0.51	43.13±1.01
240	20.53±0.12	36.22±0.35	28.99±0.86	23.46±0.51	51.2±1.00
300	25.60±0.23	47.45±0.23	36.84±0.72	30.96±0.59	65.42±2.44
360	30.89±0.23	59.62±0.11	43.83±1.09	36.29±1.37	78.12±3.04
480	36.78±0.11	78.58±0.31	56.13±1.92	49.61±1.79	98.2±1.33
600	44.01±0.23	96.28±0.63	68.04±1.20	61.06±1.67	_
720	48.05±0.20	_	83.67±0.45	74.08±1.69	_

(n=3) SD = variability in terms of the mean and the standard deviation. The average percentage of cumulative drug release varied widely across batches in various series 'F.'

Discovering the Kinetic Release of the Most Efficient Formulation

Table 19: Kinetic release data of Optimized Formulation

Time (min)	Log Time (min)	√T(min)	% Cumulative drug release	Log % Release	% Drug Remaining	Log % drug release
15	1.17	3.87	3.00	0.477	97	1.986
30	1.47	5.48	5.06	0.704	94.94	1.977
60	1.77	7.75	8.05	0.905	91.95	1.963
120	2.07	10.96	15.67	1.195	84.33	1.925
180	2.26	13.42	22.57	1.353	77.43	1.888
240	2.39	15.50	29.13	1.464	70.87	1.850
300	2.46	17.33	39.10	1.591	60.9	1.784
360	2.56	18.98	47.66	1.678	52.34	1.718
480	2.69	21.90	64.34	1.809	35.67	1.552
600	2.78	24.50	80.07	1.903	19.3	1.299
720	2.85	26.84	96.87	1.986	3.13	0.495

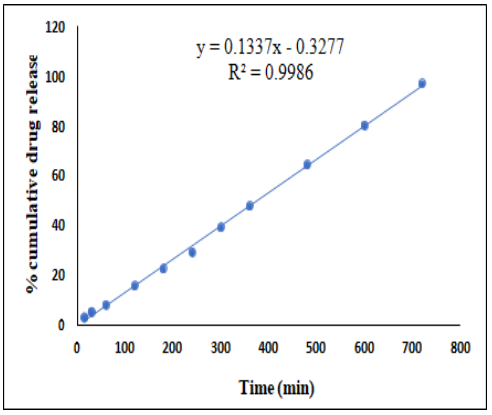


Figure : 13 Release profile of optimized formulation according to zero order

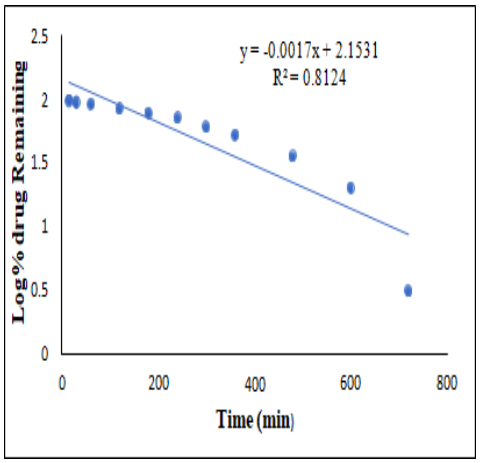


Figure 14: Release profile of optimized formulation according to first order

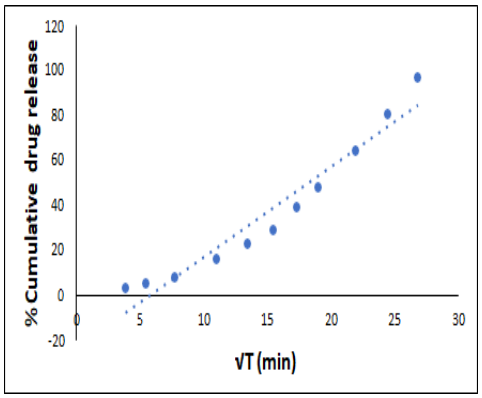


Figure 15: Release profile of Optimized Formulation according toHiguchi Diffusion

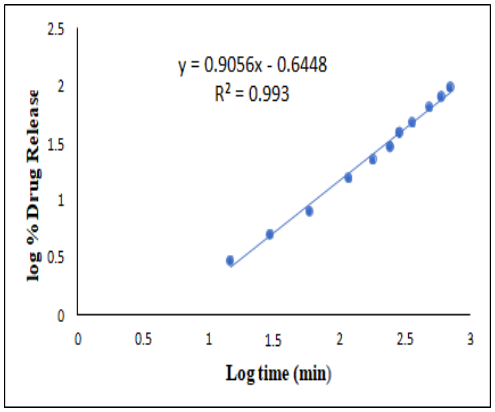


Figure16: Release profile of 0pptimized formulation according to Peppa's model

CONCLUSION

Vitamin C has been included into the design of certain drugs to improve dosing accuracy. Considering polymer choices thoroughly is necessary for the accurate design of controlled drug distribution. The present research used polymers including ethyl cellulose, cellulose acetate phthalate, and hydroxypropyl methyl cellulose to create vitamin 'C' microparticles. Ethyl cellulose, cellulose acetate phthalate, and hydroxypropyl methyl cellulose were used in an emulsion solvent evaporation method to create vitamin C microparticles. Changing the polymer ratio allowed for the creation of three distinct formulations. These formulations were subjected to a battery of analyses, including in vitro drug release studies and kinetic release as well as Fourier transform infrared spectroscopy, particle size distribution, percent practical yield, and drug entrapment efficiency. Furthermore, it was shown that increasing the polymer concentration improved encapsulation outcomes.

- According to the findings, Formulation F2 should be used as the starting point for developing a time-dependent medicine delivery system. The major purpose of this study was to analyse changes in GI symptoms over time as a function of treatment duration.
- From the results of the analyses, we may infer that:

- Vitamin C's organoleptic characteristics, physical properties, and melting point were all examined and determined to be within IP criteria throughout the preformulation research.
- They were shown to be compatible between the pure medicine and the polymer using FTIR analysis.
- The Vitamin 'C' Microparticles' size and drug entrapment effectiveness were shown to improve when polymer concentration was increased. The vitamin C content is higher in the F1 version.
- In vitro drug release investigations utilising Vitamin C Microparticles showed a controlled release pattern, which may be attributable to the Vitamin 'C' loaded onto the surface of the particles.
- Mathematical evidence from the models suggested that a zero-order model was the best fit for the release data. It has been reported that the values of the diffusion exponent 'n' for vitamin C microparticles lie between 0.5 and 0.1, indicating non-Fickian diffusion, which may be described using the Higuchi equation.
- When compared to other cellulose

derivatives, ethyl cellulose microparticles with a core:coat ratio of 1:1 were shown to have a more controlled release of vitamin 'C' over a 12-hour period.

- Using a Zero order and non-Fickian mechanism, the medicine was able to be released at a rate of 96.87 percent 12 hours later, suggesting that the F2 formulation is the best formulation.

References

[1] Ganderton D, Johnson P, Lloyd-Jones JG. 2edn, Drug Delivery Systems, Ellis Horwood, Chichester, 1987, 188-91

[2] Beckett AH. Towards better safety of drugs and pharmaceutical products. 4th ed. North Holland. Biomedical Press; 1980: 247-63.

[3] Perez MH, Siepmann J. Non-degradable microparticles containing a hydrophilic and/ or a lipophilic drug: preparation, characterization and drug release modeling. J Control Release 2003; 88: 413-28.

http://en.wikipedia.org/wiki/Microspheres.

http://www.ijrbsonline.com/files/R001.pdf/microspheres.

[4] International Journal of Research in Pharmaceutical and Biomedical Sciences 7. https://doi.org/10.1016/j.crfs.2021.03.010

Prasertmanakit S, Praphairaksit N, Chiangthong W, Muangsin N. Ethyl cellulose microcapsules for protecting and controlled release of folic acid. AAPS PharmSciTech. 2009;10(4):1104-12.

[5] Singh MN, Hemant KS, Ram M, Shivakumar HG. Microencapsulation: A promising technique for controlled drug delivery. Res Pharm Sci. 2010 Jul;5(2):65-77.

[6] Comunian T, Babazadeh A, Rehman A, Shaddel

R, Akbari-Alavijeh S, Boostani S, Jafari SM. Protection and controlled release of vitamin C by different micro/nanocarriers. Crit Rev Food Sci Nutr. 2022;62(12):3301- 3322. doi: 10.1080/10408398.2020.1865258. Epub 2020 Dec 22. PMID: 33350318.

http://www.ifrj.upm.edu.my/afjv14%281%292007/1-14.pdf

https://www.researchgate.net/publication/277520495_Ascorbic_Acid_Microencapsulation_Techniques_and_Trends-A_Review

https://www.researchgate.net/publication/257423237_Microencapsulation_of_ascorbic_acid_by_complex_coacervation_Protection_and_controlled_release

[7] Maryam Otadi,Vitamin E Micro capsulation by Ethyl cellulose Through Emulsion Solvent Evaporation Technique,World Applied Sciences Journal 14 (Special Issue of Food and Environment): 20-25,

[8] Marcela, F. , Lucía, C. , Esther, F. and Elena, M. (2016) Microencapsulation of L-Ascorbic Acid by Spray Drying Using Sodium Alginate as WallMaterial. Journal of Encapsulation and Adsorption Sciences, 6, 1-8. doi: 10.4236/jeas.2016.61001.

[9] Tuovinena L, Ruhanena E, Kinnarinen T. Starch acetate microparticles for drug delivery into retinal pigment epithelium—in vitro study. J Control Release 2004; 98: 407–13.

[10] Hart F, Boardman P. Vitamin C: A new non-steroid anti- inflammatoryagent.Br Med J 1963; 965–970.

[11] Ferreira S, Moncada S, Vane J. Vitamin C and aspirin abolish prostaglandin release from the spleen. Nat New Bio 1971; 231 (25): 237.

[12] Giles W, Bisits A. Preterm labour. The present and future of tocolysis. Best Pract Res Clin Obstet Gynaecol 2007; 21 (5): 857.

[13] Hraba´k et al. Vitamin C and aspirin abolish prostaglandin release from the spleen. Nat New Bio

2001; 231 (25): 237–239.

[14] Akbarpour F, Afrasiabi A, et al. Severe hyperkalemia caused by Vitamin C and potassium supplementation. South Med J 1985; 78(6): 756–7.

[15] Singh BN, Kim KH. Floating drug delivery systems: an approach to oral Controlled drug delivery via gastric retention. J Control Release 2000; 63:235- 59.

[16] Gennaro AR. Remington the science and practice of pharmacy. 19th ed. Philadelphia. Mack Publishing Company; 1995.

[17] Mathiowitz E. Encylopedia of controlled drug delivery. Johnwiley and Sons; Canada 1999:493-543.

Vyas SP, Khar RK. Controlled drug delivery. New Delhi. Vallabh Prakashan2002.