

## PREPARATION AND EVALUATION OF POLYHERBAL NANOSYSTEM FOR CANCER TREATMENTS

Ravindra A Sarkate\*, Research Scholar, Dept. of Pharmacy, SunRise University, Alwar  
Dr.Nandu Kayande\*\*, Professor, Dept. of Pharmacy, SunRise University, Alwar, Rajasthan, India

### Abstract:

Herbal drugs which are shows anticancer activity are selected for present study such as, *allium sativum* (Garlic), *Azardirectaindica*(Neem),*Currcuma longa*(termeric),and *Nigella sativa*(black seed oil).The aim of this study was to prepare and evaluate Herbal liquid for hard gelatine capsule.The liquid for hard gelatine capsules were prepared by using PEG 400, propylene glycol and water mixture under temp of 90<sup>0</sup> C followed by adding PVA, Cremophore EL, Labrasol and in last herbal extract finally added to the mixture under stirring.Pre-formulation study such as fourier transform infra-red spectroscopy (FTIR) evaluated. Final formulations were charecterized before filling into capsule for particle size and poly-dispersity index, zeta potential, determination of pH and viscosity.The zeta potential value is -11.1 indicates ideal physical stability of prepared herbal liquid. Viscosity of all formulation were found in the range of 65 to 95 CPS and lying withing limits from the result it was observed that viscosity increase.Hence, herbal liquid for hard gelatine capsule can be used for cancer treatments.

**Keywords:**anticancer activity,Herbal drugs,hard gelatine capsule,Nano system

### Introduction:

Malignancy persists to distinguish the leading cause of death in the human race and claims greater than 6 million lives per year [1]

An extremely potential approach to prevent cancer is chemotherapy, which is characterized as the utilization of synthetic or natural agents used alone or in combinations to obstruct the development of tumor in people. Plants, vegetables and herbs used in the folk and conventional pharmaceuticals have been acknowledged right now as one of the main wellspring of malignancy chemoprevention drug discovery and advancement [1]

Therapeutic plants have been utilized as medicine for individual diseases for a long time. The rationale behind utilizing them as a drug lies in the fact that they have chemical compositions of medicinal values.[2]

The therapeutic importance of plants lays in some chemical components usually derivative metabolites that take them into being a specific physiological accomplishment on the human being. Mainly the alkaloids, flavanoids, tannins and phenolic compounds are important biologically active metabolites responsible for the therapeutic significance.[3]

Recently, it has been observed that aged garlic extract, but not the fresh garlic extract, exhibited radical scavenging activity. The two major compounds in aged garlic, S-allylcysteine and S-allylmercapto-L-cysteine, had the highest radical scavenging activity. In addition, some organosulfur compounds derived from garlic, including S-allylcysteine, have been found to retard the growth of chemically induced and transplantable tumors in several animal models. Therefore, the consumption of garlic may provide some kind of protection from cancer development.[4]

The anticancer properties of the plant have been studied largely in terms of its preventive, protective, tumor-suppressive, immunomodulatory and apoptotic effects against various types of cancer and their molecular mechanisms.The cogent data on the anticancer biology of products from *A. indica* deserve multi-institutional clinical trials as early as possible. The prospects of relatively cheaper cancer drugs could then be brighter, particularly for the under-privileged cancer patients of the world.[5]

Curcumin, the active ingredient of the *Curcuma longa* plant, has received great attention over the past two decades as an antioxidant, anti-inflammatory, and anticancer agent. A summary of the medicinal chemistry and pharmacology of curcumin and its derivatives in regard to anticancer activity, their main mechanisms of action, and cellular targets has been provided based on the literature data from the experimental and clinical evaluation of curcumin in cancer cell lines, animal models, and human subjects.[6]

*Nigella sativa* extract, powder and seed oil and its main components, thymoquinone and  $\alpha$ -hederin, have showed potent anticancer and chemosensitizing effects against various types of cancer, such as liver, colon, breast, renal, cervical, lung, ovarian, pancreatic, prostate and skin tumors, through the modulation of various molecular signaling pathways. [7]

This liquid composition available help the most challenging drug compounds in capsules has increased significantly in recent years. In particular it is possible to solubilize many drug compounds in a micro emulsion pre-concentrate inside the hard gelatin capsules such that on subsequent dispersion in the gastro intestinal tract, the drug remains in solution. [8-11]

It is considered that this technology can make a significant contribution to the development of efficacious pharmaceutical products by providing the flexibility to rapidly develop and test in – house formulation when small quantities of drug is available. [12]

Liquid-fill hard gelatin capsule technology was established in the early 1980s as an alternative to soft gelatin capsules. This technology is mostly suitable for insoluble compounds, highly potent compounds. Once the capsule is filled, they are sealed by spraying small amount of Water/ethanol mixture at the cap and body interface followed by gentle warming to fuse the two parts of capsule together or by band sealing of capsule with gelatin or cellulose. [13,14]

### Materials and method:

#### Preparation of herbal liquid

#### Preparation of liquid formulation

To a container PEG 400 (10%), propylene glycol (10%) and water (3%) were added under stirring and heating. Product temperature was maintained at 90°. To the above step slowly PVA (4%) was added under stirring and product temperature was maintained at 90°C. To the above solution Cremophore EL (44%), Labrasol (17%) were added under stirring and heating. To the above step, Herbal extract (12%) was finally added to the mixture under stirring and heating at 90°C.

Table 1: Composition of prepared liquid diclofenac potassium

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Herbal extract	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0
Propylene Glycol	21.6	21.6	40.0	21.6	21.6	21.6	21.6	21.6	21.6
PEG 400	21.6	21.6	40.0	21.6	21.6	21.6	21.6	21.6	21.6
Water	5.8	5.8	10.0	5.8	5.8	0.0	0.0	0.0	0.0
Labrasol	70.0	70.0	70.0	70.0	35.0	35.0	35.0	35.0	35.0
Gelucire 44/14	120.0	0.0	0.0	144.0	0.0	0.0	0.0	0.0	0.0
Cremophore EL	0.0	120.0	0.0	0.0	90.0	90.0	0.0	90.0	90.0
PVP K-30	0.0	0.0	5.0	0.0	0.0	0.0	0.0	0.0	0.0
2N Hcl	0.0	0.0	0.0	0.0	0.0	12.7	1.2	0.0	3.4
Oleic acid	0.0	0.0	0.0	0.0	0.0	0.0	30.0	29.0	29.0

### Characterization of prepared herbal liquid

#### Particle size and polydispersity Index (PDI)

The particle size of prepared herbal liquid was determined by using Zetasizer version 6.20 (Malvern Instruments, Malvern, UK). All the prepared batches of prepared herbal liquid were viewed under microscope to study their size and polydispersity index (PDI). Size of herbal liquid from each batch was measured at different location on slide by taking a small drop of prepared herbal liquid solution on it and average size and PDI of prepared herbal liquid were determined. <sup>14</sup>

#### Zeta potential

This method is used to determine charge on prepared herbal liquid using Zetasizer version 6.20 (Malvern Instruments, Malvern, UK). Analysis time was kept for 60 seconds and average zeta potential and charge on the prepared herbal liquid was determined. The obtained

value will be indicates that the surface of prepared herbal liquid is dominated by the anions.  
14

**Determination of pH**

The pH of each formulation was recorded using a calibrated digital pH meter immediately after preparation. The pH of formulations was checked and noted.<sup>14</sup>

**VISCOSITY**

The viscosity of prepared herbal liquid formulation was measured by model no LVPVE Brookfield viscometer using spinder no 61 at 100 rpm.<sup>14</sup>

**Results and discussion:**

**Fourier Transform Infra-Red Spectroscopy (FTIR)**

Interaction study was performed with FTIR spectrophotometer. The FTIR spectra of herbal extract was studied.

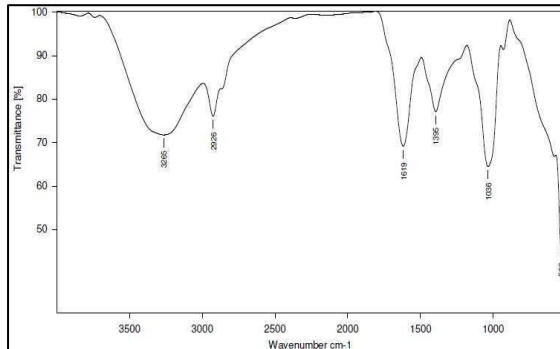


Fig 1: FTIR Spectra of *Azardirectaindica*

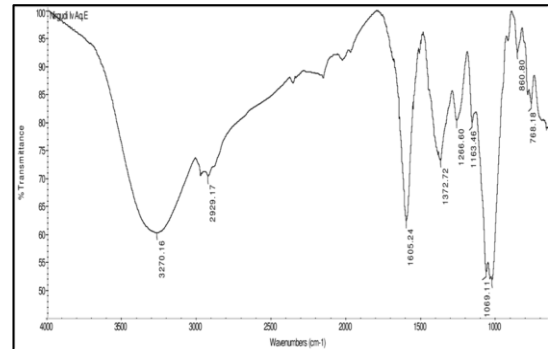


Fig 2: FTIR Spectra of *Allium sativum*

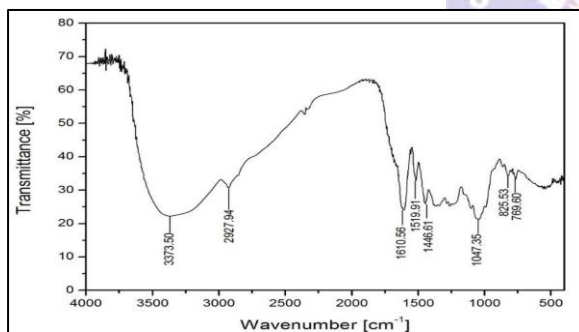


Fig 3: FTIR Spectra of *curcuma longa*

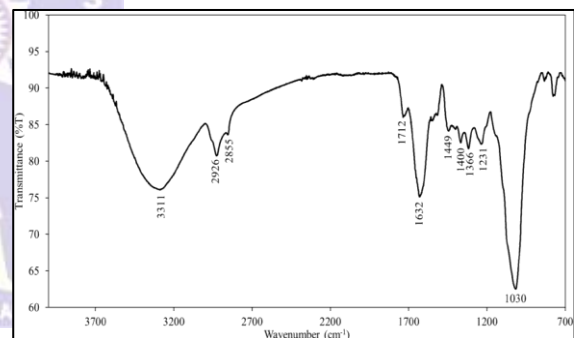


Fig 4: FTIR Spectra of *nigella sativa*

**CHARACTERIZATION OF PREPARED HERBAL LIQUID**

**Particle size and polydispersity Index (PDI)**

**Table 2:** Particle Size of Formulation.

Formulation Code	Particle Size (nm)*
F1	17.51±0.20
F2	22.97±0.44
F3	19.73±0.15
F4	15.91±0.12
F5	15.03±0.18
F6	16.49±0.21
<b>F7</b>	<b>14.80±0.30</b>
F8	20.50±0.39
F9	15.03±0.18

\* Values are articulated as mean ±SD, n=3.

**Table 3:** PDI of Formulation.

Formulation Code	PDI*
F1	0.074±0.02
F2	0.056±0.07
F3	0.040±0.04
F4	0.053±0.01
F5	0.051±0.04
F6	0.037±0.04
F7	0.031±0.04
F8	0.074±0.01
F9	0.218±0.04

\* Values are articulated as mean ±SD, n=3

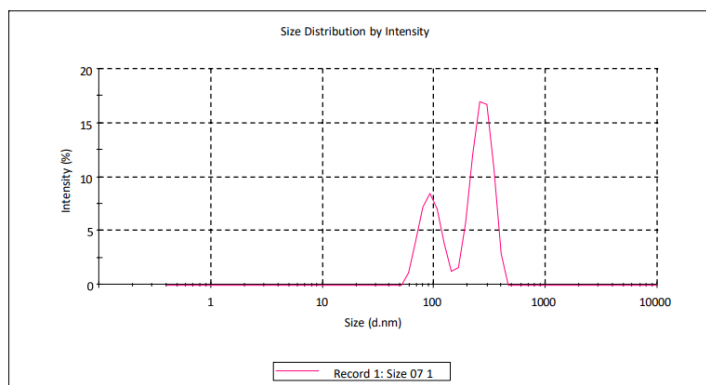


Fig 5: Particle size and polydispersity Index (PDI) (Bacth F7)

The particle size was determined by using motic microscope. All the prepared batches were viewed under microscope to study their size. All the particles were good in appearance with size particularly suitable.

**Zeta potential**

**Table 4: Zeta Potential of GOZ SNEDDS Formulation.**

Formulation Code	Zeta Potential (mV)*
F1	-4.20±0.15
F2	-3.23±0.21
F3	-2.54±0.40
F4	-8.08±0.18
F5	-7.36±0.01
F6	-5.34±0.14
<b>F7</b>	<b>-11.01±0.14</b>
F8	-5.06±0.54
F9	-6.45±0.51

\* Values are articulated as mean ±SD, n=3.

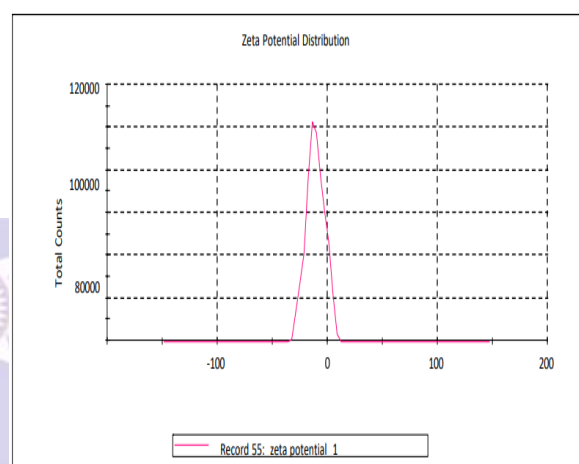


Fig 6: Zeta potential(Bacth F7)

Zeta Potential is important tool used for determination of stability and surface charges on the particles. The zeta potential value is -11.1 indicates ideal physical stability of prepared liquid diclofenac potassium.

**Determination of pH**

The pH of optimized formulation (F9) was recoded using a calibrated digital pH meter immediately after preparation. The pH of formulations was observed in the range of 6.7±0.43 to 7.15±0.90. The pH of all the formulation were in the desired range (6.7 to 7.4)

**Viscosity:**

viscosity is an expression of resistance of a fluid to flow viscosity is an important parameter for prepared liquid diclofenac potassium to be evaluated because this parameter is applicable to mixing of drug in a bulk of formulation and flow of material.

**Determination of viscosity**

FORMULATION	Viscosity Spinder no 61 (100 rpm) CPS
F1	65
F2	68
F3	72
F4	68
F5	70
F6	75
F7	76
F8	65
F9	95

Table 5 : Determination of viscosity

Viscosity of all formulation were found in the range of 65 to 95 CPS and lying withing limits from the result it was observed that viscosity increase.



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**CONCLUSION:**Herbal liquid for hard gelatin capsules has been prepared and tested. The results show that the formulation is ready for filling into hard gelatin capsules. Once the capsules are filled with hard gelatin, more research will be required. A lower dose and higher bioavailability can be used in hard gelatin capsules containing herbal liquid to achieve the desired pharmacological effect with fewer side effects.

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