

Formulation Development and Characterization of Polymeric Nanocarrier Encapsulating Phytoconstituents for The Treatment of Cancer

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Research Article

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Abstract

Herbal medications have emerged as a prominent focus within the pharmaceutical industry due to their well-established efficacy and limited occurrence of adverse effects. Moreover, in contrast to synthetic drugs, herbal medications exhibit a comparable level of interest in the production of nanoparticles. Polymeric nanoparticles have emerged as a crucial method for enhancing medication bioavailability and enabling targeted distribution to the desired location of action. Due to its medicinal properties, which include analgesic, anti-inflammatory, antibacterial, and antioxidant effects. Formulations were prepared using different ingredients using the solvent evaporation method. Polyvinyl alcohol, Polylactic acid was used as a biodegradable polymer, HPMC, Polyvinylpyrrolidone (PVP), and Sucrose. Sunitinib Malate is an active pharmaceutical ingredient that is a receptor tyrosine kinase inhibitor and chemotherapeutic drug. *Physalis peruviana* was extracted by the maceration method. The extract of the *Physalis peruviana* was encapsulated, Quercetin is the flavonoid that worked as a main constituent. The current study indicates that *Physalis peruviana*-loaded nanoparticles assist in the anti-cancer activity effectively.

1. Introduction

The WHO estimates that 80% of poor nations utilize herbal medicine for basic care [1]. Animals, marine critters, bacteria, and plants have been utilized in medicine since ancient times to prevent, diagnose and cure ailments [2]. Health treatment relies on plants, and extracts from them have been shown to be effective for certain illnesses [3]. Almost 50,000 plants are medicinal internationally. In Africa and Asia, almost 80% of the population utilizes traditional medicine for basic care. This treatment is widely used worldwide and is gaining popularity in developed countries [4]. *Physalis peruviana* (Solanaceae) is an Andean semi-upright herb shrub or perennial with branching branches. *P. peruviana* thrives at many altitudes, soils, and climates. It is the most widespread species in the *Physalis* family. Several species of *Physalis* have been used ethnomedically to treat cancer, asthma, hepatitis, dermatitis, bacterial infections, renal liver ailments, malaria, and immunomodulatory antipyretic characteristics [5]. It includes physalins, flavonoids, alkaloids, vitamins, and carotenoids, along with polysaccharides [6, 7]. The phytochemical composition of the plant is linked to its health advantages.

This research covers ethnomedicinal usage and phytoconstituents in *P. peruviana*. Nutritional values, and pharmacological data, including phytochemical characterization of isolated plant components, have been reviewed [8]. This study examined the ethnotherapeutic and phytochemical properties of *P. peruviana* L. components. Mostly for humans, *P. peruviana* treats numerous disorders. It is seldom used to treat veterinary illnesses. In the western part of Kenya, it prevents and controls cattle ticks. The plant treated the most gastrointestinal tract diseases (25.33%), which were followed by the female genital tract along with breast (13.33%), skin (9.33%), liver and biliary tract (8.01%), eye and ear (8.01%), immune system (5.33%), the endocrine system (5.33%), respiratory system (2.67%), and metabolic disorders. Joints, bones, muscles in the skeletal system, and bodily fluid abnormalities make up 1.33%. Inflammations, Helminthiasis, malaria, snake bite, fungal, bacterial, and smallpox account for 17.33%. Due to their exceptional richness, tropical nations have over 4000 species with ethnomedical evidence supporting their usage to cure [9]. Primarily, the oral route is the preferred method of medication delivery, which is determined by various formulations. The oral route of medication administration is favoured over other routes due to its advantages in terms of safety, patient compliance, simplicity of ingesting, pain avoidance, and flexibility in accommodating different kinds of

pharmaceuticals. However, in some instances (20.41% of cases), the specific course of action taken by the authorities is not clearly outlined [10]. The chemical compounds that have been found and described are derived from various components and *P. peruviana* extract. Hence, a wide range of phytoconstituents has been identified, encompassing terpenes (such as monoterpenes, sesquiterpenes, diterpenes, triterpenes, and carotenoids), phenolic compounds (including phenolic acids, phenolic esters, phenolic aldehydes, chalcones, coumarins, cinnamic acid derivatives, glucosides, and flavonoids), alcohols, ketones, aldehydes, and other carboxylic acids, steroids, lactones and withanolides, alkaloid compounds, sucrose esters, siloxanes, glucosides, nutrients, phytosterols, phytol compounds derivatives, enols, heterocycles, alkanes, benzimidazoles, alkenes, and many different functional categories [11]. Terpenes and polyphenols are the primary groups of phytoconstituents that have been found in various components of *P. peruviana*. The first value represents 26.09% whereas the second value represents 14.94%. Within the group of terpenes, carotenoids are particularly prominent, accounting for 11.15% of the total. They are followed by monoterpenes at 8.76%, sesquiterpenes at 5.57%, and diterpenes at 3.18%. Preliminary analysis of the leaf essential oil from *P. angulata*, a closely related species to *P. peruviana*, has shown the presence of a significant proportion of fatty acids (22.8%) and sesquiterpenes (22.3%) as volatile constituents.

A nanoparticulate system of combined components cape gooseberries and drug gives different effects on cancer treatment. Nanoparticles have similar characteristics that to how the drug, herbal components, and any other polymer are encapsulated or loaded in them. Gold and silver encapsulated nanoparticles are expensive and have other conventional side effects too. Nowadays nanotechnology draws the attention of researchers to the nanoparticulate system having herbal or plant-based components for the treatment due to its several benefits such as being biodegradable, less toxic to the body, cost-effective, eco-friendly, and so on. The green synthesis of nanoparticles is catching the interest of researchers for further study. Exploring more in the green synthesis field of nanoparticles for chronic diseases. To prepare the nanoparticles of *Physalis peruviana* extract loaded with the drug Sunitinib malate for the treatment of several cancers such as cervix cancer, lung carcinoma, renal cell carcinoma, and so on. For preparing the nanoparticles we have taken the fruit of *Physalis peruviana* plant. Reason for taking *Physalis peruviana* because of the several benefits such as anti-oxidant properties, anti-inflammatory properties, and good dietary supplement for the many vitamins (A, C E vitamins).

2. Materials and Methods

In this study, Sunitinib Malate was used as the drug carrier. Poly Lactic Acid (PLA), Polyvinyl Alcohol (PVA), and Hydroxypropyl methyl cellulose (HPMC) are used as polymeric carriers in the formulation. Dichloromethane (DCM) and Methanol are used as the organic solvents. The drug used was gifted by the IPCA. Sucrose and other excipients were obtained from Sigma-Aldrich. The equipment used included a probe sonicator (Labman, India), bath sonicator (Labman, India), and magnetic stirrer 2MLH (REMI, India).

2.1 Collection of Plant Material

Dried fruit *Physalis peruviana* used for the study were collected from Khari Baoli (Delhi). The fruit was recognized using its common name. *Physalis peruviana* fruit was gathered in a little bit of dried form. The

collected fruit of *Physalis peruviana* was validated (Certificate No. BSI/BGIR/1/TECH./2023/52), BGIR (Botanical Garden of Indian Republic), Sector 38, Noida, Uttar Pradesh. Pin code-201303.

2.2 Extraction of *Physalis. Peruviana*

The process in which the natural components are separated from crude medicinal products by using solvents. To separate the distinct required components from the crude medicine a proper (or combined) solvent has been extracted. The substance was removed from the solidified material. The maceration extraction was done of that solidified crushed fruit.

The maceration process is used for the extraction because of the solid and sticky nature of the fruit so only this process of extraction is possible with this. In maceration whole or coarsely powdered plant (drug) is kept in contact with the solvent in a stoppered container for a defined period with frequent agitation until the soluble matter is properly dissolved. This method is best suitable for use in the case of thermolabile drugs [12].

Table.1 Different Solvents used in the process and their storage conditions

S.NO	Solvents	Quantity	Time period	Temperature (\varvec{°C})
1.	Petroleum Ether	200ml	2 days	25–28°C
2.	Ethanol	200ml	4 days	25–28°C
3.	Methanol	200ml	4 days	25–28°C
4.	Water and Acetone (1:1)	200ml	4 days	25–28°C

2.3 Crude Drug Extract

The *Physalis peruviana* which were taken for the extraction process by maceration method has shown the yield of the following extracts shown in Table.2

Table.2 Percentage yield of *Physalis peruviana* extract in different solvents.

S. No	Name of the Extract	Nature of the drug	% Yield
1.	Petroleum ether extract	Sticky and resinous mass	11%
2.	Methanol extract	Sticky and resinous mass	76%
3.	Ethanol extract	Sticky and resinous mass	82%
4.	Acetone and water extract (1:1)	Sticky and resinous mass	40%

2.4 Phytochemical Screening of Fruit *Physalis peruviana*

The extract of *Physalis peruviana* was collected and phytochemical screening was performed using conventional reagents to verify the phytoconstituents contained.

2.5 Physicochemical properties

2.5.1 Organoleptic Properties

The physical state, colour and odour of the extract and formulation were evaluated by inspecting samples visually.

2.5.2 Solubility Studies

Solubility can be defined as the quantitative measurement of the amount of solute that can dissolve in a given solvent at a specific temperature. This phenomenon can also be described qualitatively as the rapid interaction between two or more components resulting in the formation of a homogeneous solution. The solubility of the *Physalis peruviana* extract will determine in different solvents.

Table.3 Solubility Profile of the *Physalis peruviana* extract in different solvents.

Solvents	Solubility
Methanol	Soluble
Ethanol	Soluble
Acetone	Soluble
Water	Sparingly Soluble
DMSO	Soluble
Phosphate buffer saline	Soluble

The result of solubility studied at different pH indicated that Sunitinib malate was soluble in both mediums aqueous as well as organic solvents. This may be due to the weak basic nature of Sunitinib Malate. The different values of solubilities are given below which is shown in Table.4

Table.4 Solubility Profile of Sunitinib Malate in Different Solvents

Solvents	Solubility	Values of solubility
Methanol	Soluble	10 mg/ml
Ethanol	Soluble	10 mg/ml
Acetone	Soluble	10 mg/ml
Water	Sparingly Soluble	10 mg/ml
DMSO	Soluble	10 mg/ml

2.5.3 Melting Point

At atmospheric pressure, a substance’s melting point (or, more rarely, liquefaction point) is the temperature at which it changes state from solid to liquid. The solid and liquid phases are in balance at the melting point. A substance’s melting point is determined by pressure and is generally given at standard pressure. The freezing point, also known as the crystallization point is the temperature at which a liquid change back into a solid [13].

Table.5 Melting Points of Drugs and Various Excipients

S. No	Compound	Theoretical Value	Practical Value
1.	Sunitinib Malate	189–190°C	190°C
2.	PLA	150–160°C	158°C
3.	PVA	190–200°C	198°C
4.	Sucrose	160–186°C	179°C
5.	Hydroxypropyl Methylcellulose	225–230°C	230°C

2.5.4 Interaction Studies

To find out the estimated interactions in formulations, FTIR analysis was done to find out the possible outcomes of the interaction of components during the process. FTIR spectra will be obtained by the Bruker alpha machine. The FTIR spectra of the drug, extract, and excipients are demonstrated in the result section. FTIR is used to evaluate the degradation of the polymeric matrix of the carrier system. The ATR cell caused the IR beam to be reflected multiple times throughout the sample, resulting in IR spectra that were mostly from the surface materials. The ATR-FTIR can provide details about the nanoparticles' surface composition, albeit this depends on the specifics of their synthesis [14]. The Preformulating FTIR studies of Sunitinib Malate and other different excipients used in the formulation.

2.6 Synthesis of *Physalis. peruviana* and Sunitinib Malate Nanoparticles

Synthesis of *Physalis. peruviana* combined with Sunitinib malate nanoparticles are formed by the method solvent evaporation method. Polymeric nanoparticles of Sunitinib Malate and Cape gooseberry extract were prepared by the Solvent Evaporation method. Firstly, the aqueous phase was prepared by dissolving PVA in distilled water, PVP, HPMC, PLA, Sucrose was completely dissolved in distilled water by using a bath sonicator before adding it into the organic phase with the use of a magnetic stirrer. Now, for the preparation of the organic phase, the extract and drug dissolved in methanol because of solubility and then DCM was added to it. Before the addition of the organic phase into the aqueous phase, probe sonication was done in the aqueous phase. Then the addition of organic phase in the aqueous phase dropwise on the magnetic stirrer for 8 hours for Cape gooseberry extract-containing formulations, during mixing or homogenization, Cape gooseberry extract was also added in the organic phase.

The solvent method for preparing polymeric nanoparticles encapsulating phytoconstituent.

2.6.1 Preparation of materials – Collect the required materials including drug, PVA, PLA, HPMC, sucrose, extracted form of phytoconstituent, organic solvents, and glass apparatuses.

2.6.2 Weighing and Mixing – Weighing and mixing of materials as per the process. The two phases are mixed separately and then those phases are mixed together with the help of a syringe or dropper.

2.6.3 Sonication - Proper sonication is done with the help of a probe sonicator. Probe sonication is done for the mixing of the polymers, the formation of nanoparticles, and reducing the size.

2.6.4 Reduction of Size and Evaporation of Organic Solvent- Evaporation of the solvents is done during the size reduction process. The formed polymeric nanoparticles were placed on the magnetic stirrer for a few hours so that the shaping of the nanoparticles will take place along with the solvent evaporation.

2.7 Formulation Development of Nanoparticles

Table.6 Composition of Formulations

Code	Sunitinib Malate (mg)	Ext. (ml)	PLA (mg)	PVA (mg)	PVP (mg)	HPMC (mg)	Sucrose (gm)	Methanol (ml)	DCM (ml)	D.W (ml)
F0	-	-	50	160	250	100	1	2	2	16
F1	-	-	50	160	250	100	-	2	2	16
F2	-	2	50	160	250	100	1	2	2	16
F3	-	2	50	160	250	100	-	2	2	16
F4	-	2	-	160	250	100	-	2	2	16
F5	5	-	50	160	250	100	1	2	2	16
F6	5	-	50	160	250	100	1	2	2	16
F7	5	-	50	160	250	100	-	2	2	16
F8	5	-	50	160	250	100	-	2	2	16
F9	5	-	50	160	250	100	1	2	2	16
F10	5	2	50	160	250	100	1	2	2	16
F11	5	2	-	160	250	100	-	2	2	16
F12	5	2	50	160	250	50	-	2	2	16
F13	5	2	50	160	250	50	1	2	2	16

2.8 Characterization of Physalis. peruviana and Sunitinib Malate Nanoparticles

2.8.1 Morphological analysis

2.8.1.1 Optical Microscopy

The prepared formulation was observed under a microscope at a magnification of 45x, revealing the presence of round or spherical-shaped vesicles with distinctive projections.

2.8.1.2 Scanning Electron Microscopy

The morphology of the surface and molecule size of polymeric nanoparticles were determined by Scanning Electron Microscopy using. Dried nanoparticles were kept on an electron-magnifying lens metal stub and covered with gold in a falter [15]. Picture of the nanoparticle was taken by arbitrary checking of the stub. Surface characterization and Morphology are additionally maintained by SEM. The examples for the SEM investigation were ready by sprinkling the nanoparticles on one side of the twofold glue stub. The stub was then covered with a fine gold residue. The nanoparticles will be seen with the SEM [16].

2.9 Evaluations of Formulated Formulation Batches

2.9.1 Percentage Yield and Entrapment Efficiency Determination

By measuring the concentration of untrapped drugs in an aqueous medium, the entrapment effectiveness of the produced Polymeric nanoparticles was determined using centrifugation. Using a REMI cooling centrifuge, the produced polymeric nanoparticles dispersion was centrifuged at 25000 rpm for 30 minutes at 6°C. By maintaining the polymeric nanoparticles in the buffer solution and allowing them to lyse, the entrapment efficiency or percent entrapment of the polymeric nanoparticles may be measured. The resulting lysate is filtered or centrifuged before being subjected to the monograph-required determination of active components [17]. The entrapment efficiency and % yield of Nanoparticles was calculated by using the following formulas [18].

Entrapment efficiency (%) = (Calculated drug content / Theoretical drug content) × 100

Yield (%) = (Weight of PNs /Total expected weight of drug and polymer) × 100

2.9.2 Drug Content

1ml of produced polymeric nanoparticle formulation is dissolved in 10 ml of pH 7.4 phosphate buffer solution (PBS) and methanol combination. A UV spectrophotometer set at 425 nm was used to measure the drug concentration in the system. As a comparison, the drug-laden polymeric nanoparticle is loaded with a placebo formulation as the control. The entire amount of drug content was figured out.

2.9.3 Stability Studies

Stability study was done a different customized and modified the demonstrated procedures. Nanoparticles formulation along with extracts of *Physalis. peruviana* were sealed in a transparent chamber or flask with a proper exposure of light and other amber glass flasks covered with aluminium foil not in the presence of light. After that these were kept in the refrigerator ($7 \pm 0.5^\circ\text{C}$) and at room temperature ($25 \pm 0.5^\circ\text{C}$). The evaluation was done for a stable period of time duration of 120 days. The parameters which were checked were zeta potential, pH, drug content, and *in-vitro* release [19].

2.9.4 Determination of Zeta-potential, particle size, and Polydispersity index of formulations.

Zeta potential, particle size, and polydispersity index are the important parameters of the evaluation. Zeta potential measures the electric potential difference at the particle surface, while particle size indicates the size of individual particles. The zeta potential is indicative of the surface potential of particles, and it is affected by alterations in their interaction with the dispersing agent in the environment. These alterations can arise from the disassociation of functional categories on the particle's surface or due to the adsorption of ionic compounds found in the water-based dispersion medium [20].

2.9.5 In-Vitro Release

The dialysis bag technique was used to conduct *in-vitro* release experiments of prepared polymeric nanoparticles. A dialysis bag was cleaned and left for soaking in distilled water. A measured quantity of polymeric nanoparticles was placed in the dialysis sac and was sealed with the aid of thread. After sealing the dialysis bag, it was placed in a beaker with 500 ml of PBS pH 7.4. The temperature was maintained at $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ by placing the beaker over a magnetic stirrer (50 rpm). At intervals of time, samples were taken. Throughout the procedure, the sink state was maintained by substituting the withdrawn sample with fresh PBS. Samples were diluted and using a UV-visible spectrophotometer at 231 nm, drug content was determined.

2.9.6 Fourier Transform Infrared (FTIR) Spectroscopic Analysis

The FTIR of prepared polymeric nanoparticles was done by ATR, Alpha (Bruker), and FTIR spectrophotometer in the range of $4000\text{--}659\text{cm}^{-1}$. The deterioration of the carrier system's polymeric matrix is measured using FTIR. The IR beam traveling through the ATR cell reflected numerous times through the sample, yielding mostly surface material IR spectra. Depending on the manufacturing techniques and conditions, the ATR-FTIR offers information about the surface composition of nanoparticles. FTIR is utilized to decide the debasement of the polymeric framework of the transporter framework. The outer layer of the nanoparticles is examined estimating Attenuated Total Reflectance (ATR). The IR bar going through the ATR cell is reflected ordinarily through the example to give IR spectra principally of surface material. The ATR-FTIR gives data about the surface creation of the nanoparticles relying on assembling systems and conditions. The FTIR of an optimized batch of Polymeric nanoparticles (F2) with methanolic extract of *Physalis peruviana*.

3. Result and Discussions

3.1 Phytochemical Investigation of *Physalis peruviana*

Crude Drug Extract

The *Physalis peruviana* which were taken out by the maceration process has shown the yield of the following extracts are mentioned in Table.2

3.2 Preliminary Phytochemical Screening

Table.7 Phytochemical screening of *Physalis Peruviana*

Phytoconstituents	Petroleum ether extract	Methanol extract	Ethanol extract	Acetone and water extract (1:1)
Carbohydrate	Absent	Absent	Absent	Absent
Alkaloids	Present	Present	Present	Present
Tannins	Absent	Present	Present	Absent
Glycosides	Absent	Present	Present	Absent
Saponins	Absent	Present	Present	Present
Flavonoids	Present	Present	Present	Present
Steroids	Absent	Absent	Absent	Absent
Proteins	Absent	Present	Absent	Absent
Amino acids	Absent	Absent	Absent	Absent
Phenolic	Present	Present	Present	Absent
Gums and mucilage	Absent	Absent	Absent	Absent
Vitamin C	Absent	Present	Present	Present

3.3 Characterization of Physalis. peruviana and Sunitinib Malate Nanoparticles

3.1 Morphological analysis

3.1.1 Optical microscopy

The prepared formulation was observed under a microscope at a magnification of 45x, revealing the presence of round or spherical-shaped vesicles with distinctive projections.

3.1.2 Scanning Electron Microscopy (SEM)

The SEM images were seen for the optimized formulations. The results are shown in the figure.2

3.3 Evaluations of Formulations

3.3.1 Stability Studies

In stability studies the formulations were kept in different conditions to check out the stability of the formulations. For finding out the compatible formulation stability studies should be done. Formulations were kept in different places like a room temperature (25°C) with the presence of light incidence, refrigeration with

the presence of light incidence (7 °C), room temperature (25°C) in a dark room, and refrigeration with no presence of light (7 °C), monitored for 120 days at proper time intervals. It was observed that the more oxidation and reduction in the pH was seen in the formulations which were place at the room temperature ($p < 0.05$) and the rest formulations had the little bit acidic Ph (5.39 ± 0.08).

3.3.2 Percentage Yield and Entrapment Efficiency

Keeping the strong Polymeric nanoparticles in the cushion configuration and allowing lysing controls capture productivity and percent entanglement. The lysate is centrifuged and then oppressed to ensure dynamic components according to the monograph. The following formulas determined PN entanglement effectiveness and yield.

Drug loading (%) = *Amount of drugs loaded in complex/Total weight of complex × 100.*

Entrapment efficiency (%) = *Weight of drugs added – Free drugs in supernatants/Weight of drugs added × 100.*

Table.8 Percentage yield and entrapment efficiency of the batches

Batches	Percentage Yield (%)	Entrapment efficiency (%)
F1	55.4	45.65
F2	65.25	58.21
F3	70.64	65.23
F4	58.95	69.12
F5	49.25	70.86
F6	70.15	65.27
F7	55.45	59.98
F8	60.11	74.29
F9	68.34	76.85
F10	48.26	50.56
F11	60.42	59.24
F12	70.58	69.83
F13	67.69	60.75

3.3.3 In- vitro drug release study

Table.9 Percentage of drug release

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13
0	0	0	0	0	0	0	0	0	0	0	0	0	0
60	13.4	12.7	16.4	13.5	13.9	14.2	15.4	15.7	12.4	12.7	15.6	14.3	18.2
120	20.1	21.4	23.5	22.9	21.2	22.9	22.4	19.5	20.4	22.4	22.1	21.5	29.5
180	27.3	28.4	29.1	31.8	30.2	32.8	31.2	30.3	28.2	31.4	34.5	34.8	37.6
240	32.9	34.4	38.1	36.5	37.4	38.1	37.9	36.4	39.4	38.7	41.2	42.5	42.5
300	42.3	44.2	46.1	47.2	48.1	49.9	48.2	47.3	48.5	47.3	50.5	51.9	56.2
360	50.2	51.3	52.3	49.6	49.4	50.4	50.8	51.6	54.5	57.9	62.7	62.4	65.9
420	61.9	62.4	64.1	62.8	60.8	63.5	64.3	62.8	65.5	68.9	71.6	72.6	71.3
480	68.3	69.2	70.1	70.7	71.4	72.1	73.1	72.5	73.4	74.9	77.4	77.8	81.3
540	71.6	72.3	74.6	73.9	74.8	75.9	76.2	76.9	76.8	78.5	80.3	83.2	87.4
600	80.9	83.2	84.7	85.1	86.3	85.2	84.2	80.2	81.9	80.2	86.8	87.4	90.4
660	81.6	84.3	85.2	85.6	86.8	85.9	84.6	80.5	81.8	80.3	86.2	87.3	90.6
720	81.5	83.9	85.5	85.8	86.2	86.1	84.2	81.1	81.9	80.4	85.9	87.5	90.3

3.3.4 FTIR of *Physalis Peruviana*, Formulation Batches, Excipients and Drug.

FT-IR, as the other absorbance-based analytical technique was used to the characterization of synthesis quality by identifying organic and polymeric compounds. In FT-IR analyses, surface-modified and drug entrapped nanoparticles samples were analysed and results were processed using the software FT-IR spectrum.

3.3.4.1 FTIR study of plant extracts

Table.10 IR Interpretation of Methanolic Extract of *Physalis Peruviana*

Peak Range	Group	class	Frequencies Determined
735–775	C-H stretching	alkene (1,2-disubstituted)	773.36
985–995	C = C stretching	primary alcohol	987.69
1030–1070	S = O stretching	sulfoxide	1058.35
1250–1310	C-O stretching	aromatic ester	1251.57
1300–1350	S = O stretching	sulfone	1341.26
1600–1650	C = C stretching	conjugated alkene	1643.96
2840–3000	C-H stretching	alkane	2879.67
2500–3300	O-H stretching	carboxylic acid	3216.22

Table.11 IR Interpretation of Ethanolic Extract of *Physalis Peruviana*

Peak Range	Group	class	Frequencies Determined
735–775	C-H stretching	alkene (1,2-disubstituted)	774.57
790–840	C = C stretching	alkene	820.08
990–1050	P-O-C stretching	aliphatic phosphates	1012.22
1000–1410	S = O stretching	sulfonyl chloride	1066.24
1087–1124	C-O stretching	Secondary alcohol	1111.45
1020–1250	C-N stretching	amine	1240.95
1335–1370	S = O stretching	sulphonamide	1352.06
2840–3000	C-H stretching	alkane	2933.11
2500–3300	O-H stretching	carboxylic acid	3241.32

Table.12 IR Interpretation of Acetone and Water Extract of *Physalis Peruviana*

Peak Range	Group	class	Frequencies Determined
760–800	C-H stretching	alkene (1,2-disubstituted)	775.69
790–840	C = C stretching	alkene	872.80
990–1050	P-O-C stretching	aliphatic phosphates	923.69
1020–1090	N-H stretching	primary amine	1025.97
1000–1410	S = O stretching	sulfonyl chloride	1327.78
1370–1420	S-O stretching	organic sulphates	1403.60
2500–3300	O-H stretching	carboxylic acid	3221.63

3.3.4.2 FTIR study of excipients used

Table.13 IR Interpretation of HPMC (Hydroxypropyl Methyl Cellulose)

Peak Range	Group	class	Frequencies Determined
1050–1085	C-O stretching	primary alcohol	1052.85
1500–1550	N-O stretching	nitro compound	1518.19
1800–2100	C = O stretching	carbonyl compound	1895.38
3700–3900	O-H stretching	alcohol	3743.44
3700–3900	O-H stretching	alcohol	3885.39

Table.14 IR Interpretation of PVA (Poly Vinyl Alcohol)

Peak Range	Group	class	Frequencies Determined
665–730	C = C stretching	alkene	696.29
925–1005	C = C stretching	Cyclohexane rings	938.85
1410–1490	O-C stretching	carbonate ion	1422.22
1485–1555	N-N stretching	aromatic nitro compounds	1516.14
1725–1740	C = O stretching	carbonyl compound (aldehyde)	1746.13
2275–2349	N = C = O stretching	isocyanate	2318.89
3584–3700	O-H stretching	alcohol	3613.14
3700–3900	O-H stretching	alcohol	3753.36
3700–3900	O-H stretching	alcohol	3871.98

Table.15 IR Interpretation of Sucrose

Peak Range	Group	Class	Frequencies Determined
630–660	CH ₃ -S-(C-S) stretching	thioethers	659.22
820–890	C-H stretching	1,3-disubstituted	856.40
670–900	C-H stretching	aromatic	905.71
925–1005	Methylene-CH ₂ stretching	cyclohexane	987.15
1000–1055	Methylene -CH ₂ stretching	cyclohexane ring vibrations	1045.61
1330–1350	C-H stretching	methylene	1346.75
1450–1510	C = C-C stretching	aromatic ring	1502.71
1725–1750	C = O stretching	ester carbonyl compound	1741.80
2915–2935	C-H stretching	methylene	2932.50
3200–3400	O-H stretching	alcohol	3345.50
3200–3570	O-H stretching	alcohol	3516.58
3584–3700	O-H stretching	alcohol	3666.83

Table.16 IR Interpretation of Drug

Peak Range	Group	Class	Frequencies Determined
630–660	CH ₃ -S-(C-S) stretching	thioethers	659.80
790–840	C = C stretching	alkene	799.92
1020–1090	N-H stretching	primary amine	1028.53
1087–1124	C-O stretching	primary alcohol	1099.54
1163–1210	C-O stretching	Ester	1190.63
1300–1350	S = O stretching	sulfone	1318.10
1465–1500	C-H bending	alkane	1472.50
1500–1550	N-O stretching	nitro compound	1525.32
1566–1650	C = C stretching	cyclic alkene	1569.77
1580–1650	N-H bending	amine	1631.89
1668–1678	C = C stretching	alkene	1678.06
3200–3550	O-H stretching	alcohol	3224.96
3584–3700	O-H stretching	alcohol	3746.15

3.3.4.3 FTIR study of Formulated batches

Table.17 IR interpretation of Formulation batch of *Physalis Peruviana*

Peak Range	Group	class	Frequencies Determined
1626–1662	C = C stretching	alkene	1638.50
3200–3550	O-H stretching	primary alcohol	3224.42

Table.18 IR interpretation of formulation batch of drug (F11)

Peak Range	Group	class	Frequencies Determined
1626–1662	C = C stretching	alkene	1637.81
3200–3550	O-H stretching	primary alcohol	3224.42

Table.19 IR of formulation batch of drug and extract (F13)

Peak Range	Group	class	Frequencies Determined
665–730	C = C bending	alkene	639.02
790–840	C = C bending	alkene	811.79
870–895	C = C bending	alkene	873.96
1000–1400	C-F stretching	fluoro compound	1016.14
1266–1342	C-N stretching	aromatic amine	1290.82
1330–1420	O-H bending	alcohol	1414.66
1450	C-H bending	alkane	1450.00
1626–1662	C = C stretching	alkene	1662.93
2840 – 2830	C-H stretching	alkane	2842.51
			2950.02
3200–3550	O-H stretching	primary alcohol	3254.64
3415 – 3380	N-H stretching	aromatic amine	3728.00

3.3.5 UV- Spectrophotometric study

Determination of Wavelength of *Physalis Peruviana*

Table.20 Determination of Wavelength of *Physalis Peruviana* extract.

No.	P/V	Wavelength	Abs.	Description
1		282.20	0.529	
2		250.40	0.331	

Table.21 Absorbance table of *Physalis Peruviana* extract standard curve in water.

Sample ID	Ex	Conc.	WL282.0	Wgt. Factor
1	Standard	0.000	0.00	1.000
2	Standard	2.000	0.022	1.000
3	Standard	4.000	0.050	1.000
4	Standard	6.000	0.074	1.000
5	Standard	8.000	0.101	1.000
6	Standard	10.000	0.128	1.000

Table.22 Absorbance table of *Physalis Peruviana* extract standard curve in methanol.

Sample ID	Ex	Conc.	WL282.0	Wgt. Factor
1	Standard	0.000	0.000	1.000
2	Standard	2.000	0.055	1.000
3	Standard	4.000	0.105	1.000
4	Standard	6.000	0.154	1.000
5	Standard	8.000	0.205	1.000
6	Standard	10.000	0.250	1.000

Table.23 Absorbance table of *Physalis Peruviana* extract standard curve in ethanol.

Sample ID	Ex	Conc.	WL282.0	Wgt. Factor
1	Standard	0.000	0.000	1.000
2	Standard	2.000	0.11	1.000
3	Standard	4.000	0.200	1.000
4	Standard	6.000	0.320	1.000
5	Standard	8.000	0.417	1.000
6	Standard	10.000	0.530	1.000

Table 24
Absorbance table of *Physalis Peruviana* extract standard curve
in DMSO.

Sample ID	Ex	Conc.	WL282.0	Wgt. Factor
1	Standard	0.000	0.000	1.000
2	Standard	2.000	0.039	1.000
3	Standard	4.000	0.084	1.000
4	Standard	6.000	0.121	1.000
5	Standard	8.000	0.167	1.000
6	Standard	10.000	0.211	1.000

Table.25 Absorbance table of *Physalis Peruviana* extract standard curve in phosphate buffer.

Sample ID	Ex	Conc.	WL282.0	Wgt. Factor
1	Standard	0.000	0.000	1.000
2	Standard	2.000	0.070	1.000
3	Standard	4.000	0.151	1.000
4	Standard	6.000	0.223	1.000
5	Standard	8.000	0.304	1.000
6	Standard	10.000	0.373	1.000

Table.26 Sunitinib Malate standard curve in methanol.

Sample ID	Ex	Conc.	WL428.0	Wgt. Factor
1	Standard	0.000	0.000	1.000
2	Standard	2.000	0.128	1.000
3	Standard	4.000	0.360	1.000
4	Standard	6.000	0.579	1.000
5	Standard	8.000	0.793	1.000
6	Standard	10.000	1.030	1.000

Table.27 Standard curve of Sunitinib Malate in phosphate buffer.

Sample ID	Ex	Conc.	WL428.0	Wgt. Factor
1	Standard	0.000	0.000	1.000
2	Standard	2.000	0.207	1.000
3	Standard	4.000	0.378	1.000
4	Standard	6.000	0.595	1.000
5	Standard	8.000	0.812	1.000
6	Standard	10.000	1.007	1.000

Table.28 Standard curve of Sunitinib Malate in water.

Sample ID	Ex	Conc.	WL428.0	Wgt. Factor
1	Standard	0.000	0.000	1.000
2	Standard	2.000	0.194	1.000
3	Standard	4.000	0.365	1.000
4	Standard	6.000	0.565	1.000
5	Standard	8.000	0.803	1.000
6	Standard	10.000	1.012	1.000

3.3.6 Zeta-potential, particle size and Polydispersity index of formulations.

Zeta potential, particle size, and Polydispersity index are the important parameters of the evaluation. Zeta potential measures the electric potential difference at the particle surface, while particle size indicates the size of individual particles. The table of particle sizes and potential is shown below, and the Polydispersity Index's inclusion offers details on the distribution of particle sizes within each formulation. A greater PDI number reflects a wider variety of particle sizes within the formulation, while a lower value denotes a more uniform particle size distribution.

Table .29 Particle Size Distribution statistical table of the formulated batch (F13)

Statistics Table						
Name	Mean	Standard Deviation	RSD	Minimum	Maximum	
Z-Average (nm)	293	-	-	293	293	
Polydispersity Index (PI)	0.1883	-	-	0.1883	0.1883	
Intercept	0.9412	-	-	0.9412	0.9412	
Derived Mean Count Rate (kcps)	3235	-	-	3235	3235	
Cuvette Position (mm)	4.64	-	-	4.64	4.64	
Number Of Size Runs	30	-	-	30	30	
Run Retention (%)	100	-	-	100	100	
In Range (%)	92.08	-	-	92.08	92.08	
Fit Error	0.001372	-	-	0.001372	0.001372	
Detector Angle (°)	90	-	-	90	90	

Table. 30 Zeta Potential statistical table of the formulated batch (F13).

Name	Mean	Standard Deviation	RSD	Minimum	Maximum	
Zeta Potential (mV)	-11.66	-	-	-11.66	-11.66	
Zeta Deviation (mV)	5.751	-	-	5.751	5.751	
Conductivity (mS/cm)	0.6068	-	-	0.6068	0.6068	
Quality Factor	3.705	-	-	3.705	3.705	
Number Of Zeta Runs	12	-	-	12	12	
Mean Count Rate (kcps)	560.7	-	-	560.7	560.7	
Reference Beam Count Rate (kcps)	2486	-	-	2486	2486	
Effective Voltage (V)	149.8	-	-	149.8	149.8	
Measured Current (mA)	1.376	-	-	1.376	1.376	
Wall Zeta Potential (mV)	-5.218	-	-	-5.218	-5.218	
Attenuator	7	-	-	7	7	

Table.31 Average size, zeta potential, and polydispersity index of formulation batches from F1-F13.

Sr. No.	Batch No.	Z-Average (nm)	Polydispersity index	Zeta potential (mv)
1.	F1	460	0.2445	-7.85
2.	F2	457.9	0.2634	-9.91
3.	F3	397	0.2535	-9.68
4.	F4	388	0.1999	-14.37
5.	F5	353.5	0.2531	-14.53
6.	F6	451.0	0.2497	-13.90
7.	F7	364.1	0.2486	-15.86
8.	F8	359.2	0.2243	-13.80
9.	F9	355.3	0.222	13.18
10.	F10	349	0.1944	12.33
11.	F11	328.1	0.1923	-12.47
12.	F12	310	0.1894	-12.02
13.	F13	293	0.1883	-11.66

3.3.7 Cell Study

3.3.7.1 MTT Assay for finding out the effectiveness of the formulation and cytotoxicity

The cytotoxicity of Sunitinib malate and *Physalis. Peruviana* extract were determined on the A549 cell line by the MTT (3-(4, 5-dimethyl thiazol-2yl)-2, 5-diphenyl tetrazolium bromide) assay. 1×10^5 /well cells were plated in 96-well plates for 24hr. the treatment was given to the cells for 24hr. after the incubation, 100 μ l of MTT dye (5mg/ml) was added to each well. The plates were incubated for 3-4hrs in an incubator for the formation of formazan crystals. After incubation, 100 μ l of DMSO (solubilizing reagent) was added to each well and mixed well by micropipette, and left for 10-15minute. The presence of viable cells was visualized by the development of purple colour due to the formation of formazan crystals. The absorbance was measured by a spectrophotometer at 268nm.

3.3.7.2 Result

To determine the cytotoxicity, A549 cells were incubated with varying concentrations (200 μ g/ml–600 μ g/ml) of the *Physalis. peruviana* extract and anti-cancerous drug Sunitinib malate. The MTT assay was utilized to assess the viability in terms of cell death. Cell death was increased in a concentration and time-dependent manner following the exposure of samples. The extract induced cell cytotoxicity in a concentration-dependent manner, as illustrated. The extract was showed inhibit the proliferation of the cancer cells A549 when compared with control. The viability was expressed in a statistically significant dose-dependent manner. The

extract of *Physalis. peruviana* was most potent for anti-cancerous activity in human lung cancer cell line are shown in Figure.26

Conclusion

In conclusion, developing and characterizing polymeric nanocarriers containing phytoconstituents for cervical cancer therapy has enormous potential to advance treatment. The polymeric nanocarriers successfully included plant extract and sunitinib malate, enabling combination therapeutic benefits. The nanocarriers have regulated release profiles, particle size, surface charge, and shape. These results suggest that the nanocarriers can deliver tailored drugs for cervical cancer therapy. This research lays the groundwork for cellular uptake, cytotoxicity, and in vivo cervical cancer cell line and animal model studies. Nanocarrier therapeutic effectiveness may be improved by optimizing formulation and characterization. Polymeric nanocarriers promote medication stability, controlled release, and targeted distribution on the site of action. Nanocarriers containing phytoconstituents with anticancer characteristics have increased therapeutic potential. These nanocarriers may improve cervical cancer therapy by combining phytochemicals with sunitinib malate. Formulation and characterization of polymeric nanocarriers containing phytoconstituents are potential cervical cancer treatments. This thesis opens the door to nanocarrier research, optimization, and clinical use. The potential advantages of greater treatment effectiveness, fewer side effects, and improved patient outcomes make nanocarrier investigation and development crucial in cervical cancer therapy.

Abbreviations

P.P

Physalis. Peruviana

SEM

Scanning Electron Microscopy

FTIR

Fourier Transform Infrared

Declarations

FINANCIAL SUPPORT

There is no financial support is required for this review article.

CONFLICT OF INTERESTS

The authors declared no conflict of interest.

RESEARCH INVOLVING HUMAN PARTICIPANTS AND/OR ANIMALS

This article does not contain any studies with human participants or animals performed by any of the authors.

INFORMED CONSENT

We affirm that all the authors have seen, prepared, and agreed to the submission of the paper and their inclusion of name(s) as co-author(s).

FUNDING / SUPPORT

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Figures

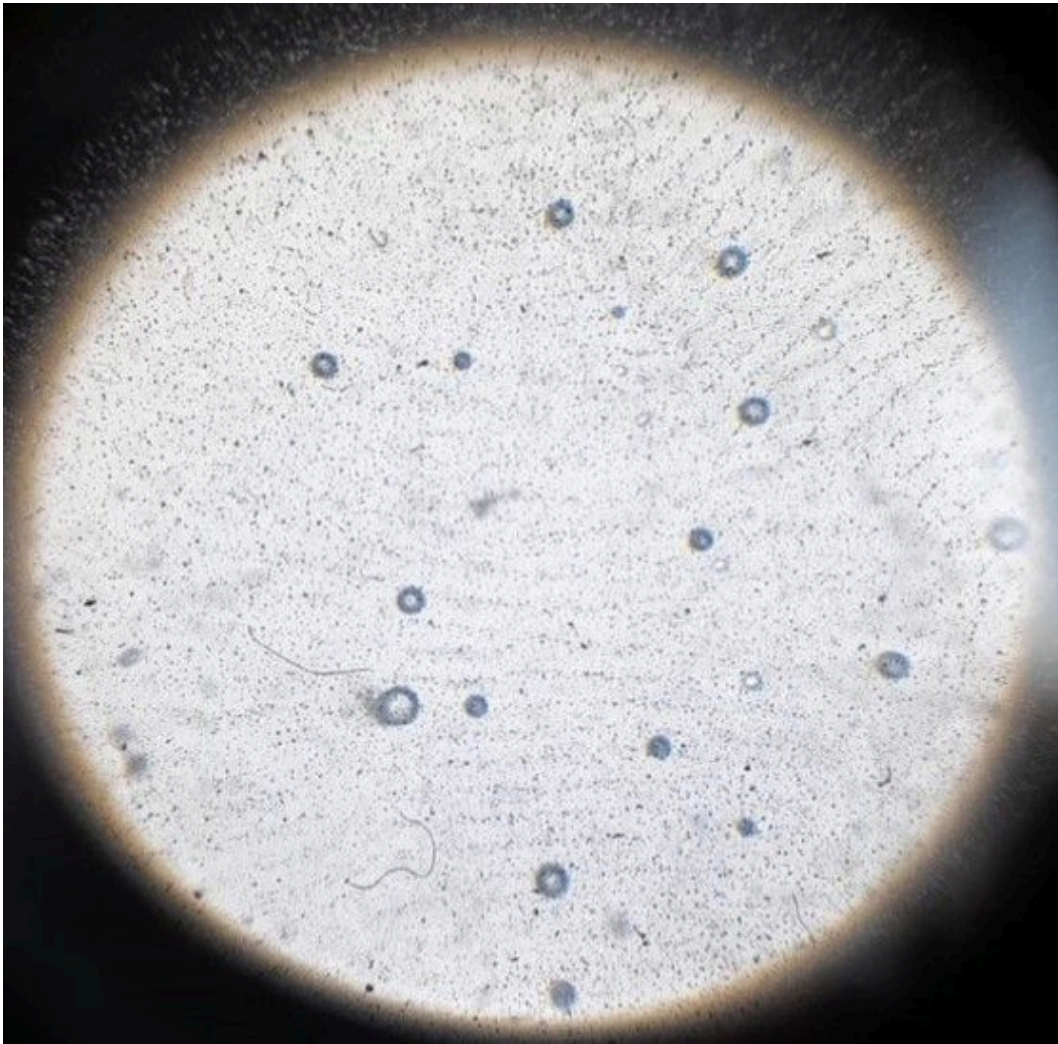


Figure 1

Optical Microscopy of batch F13

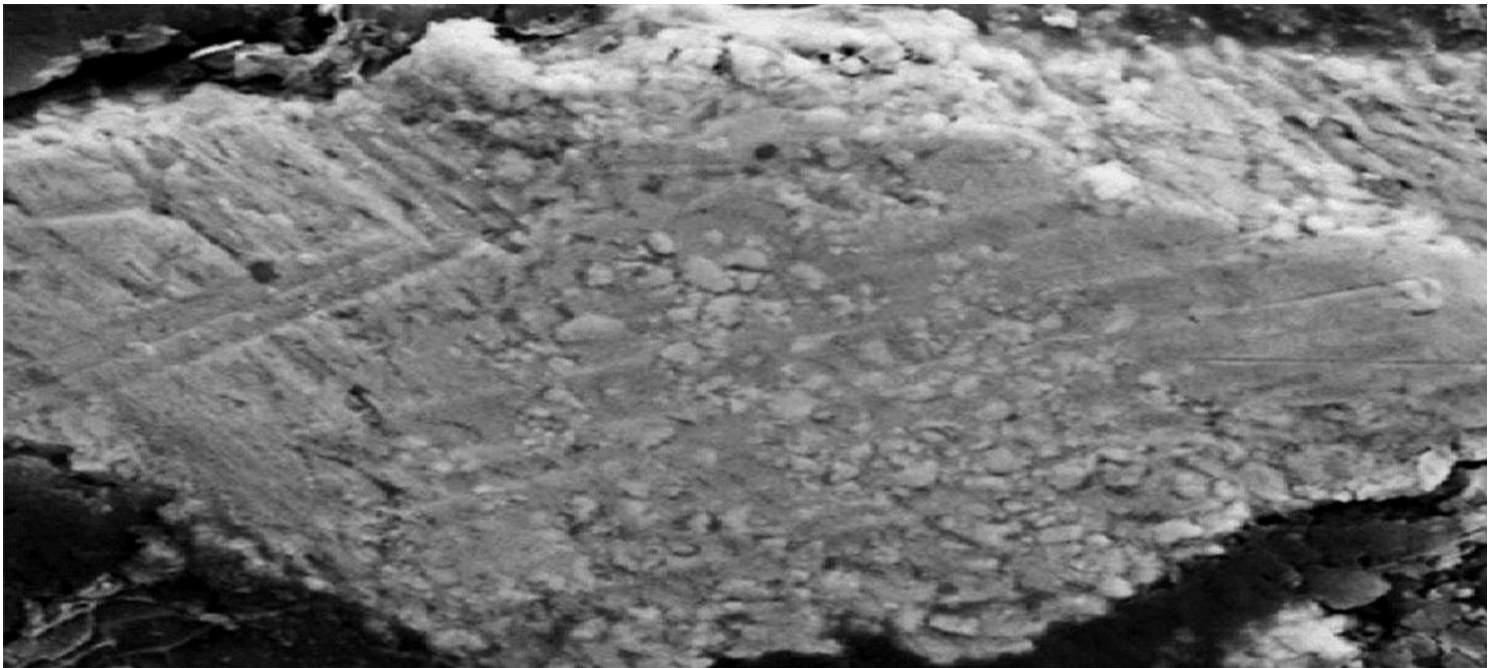


Figure 2

SEM Image of Optimized Polymeric Nanoparticles Formulation Batches (F13)

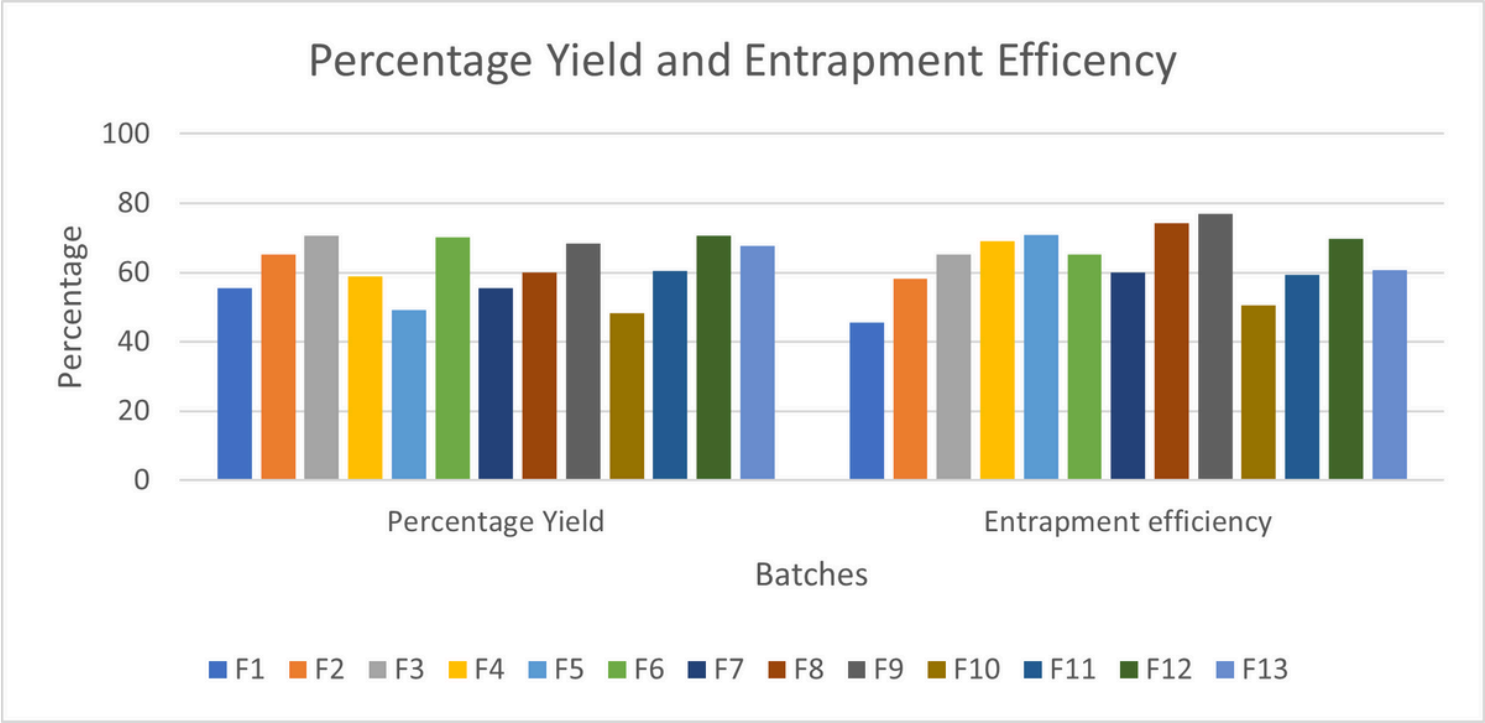


Figure 3

Column representation of percentage yield & entrapment efficiency of batch F1-F13.

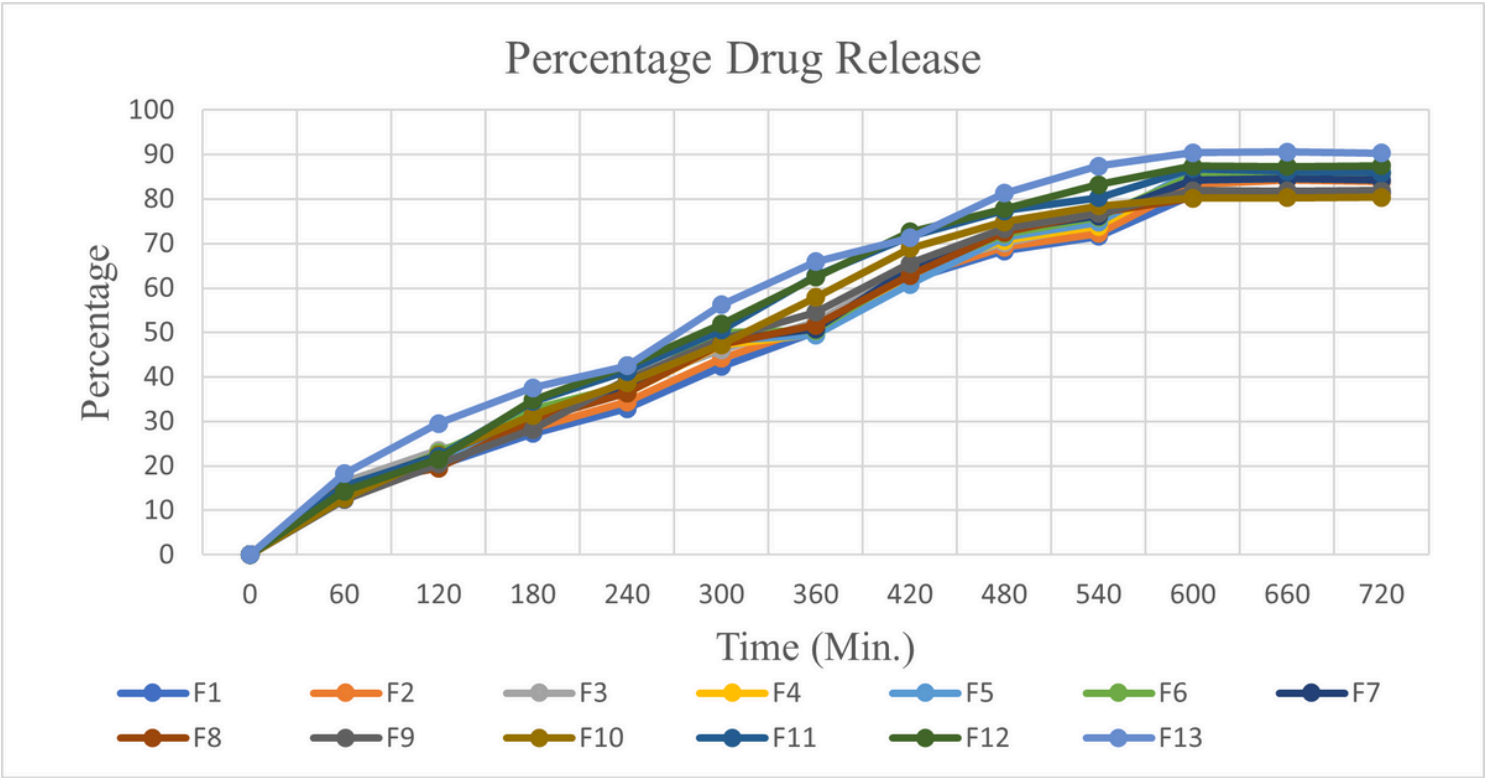


Figure 4

Percentage of drug release of different batches (F1-F13)

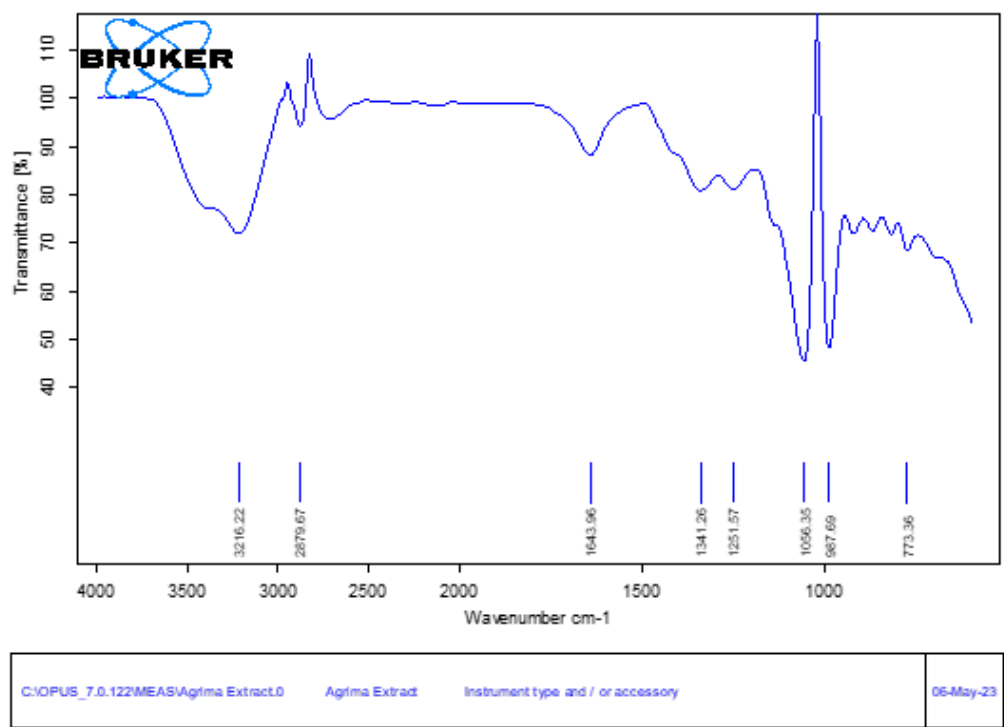


Figure 5

IR of Methanolic Extract of *Physalis Peruviana*

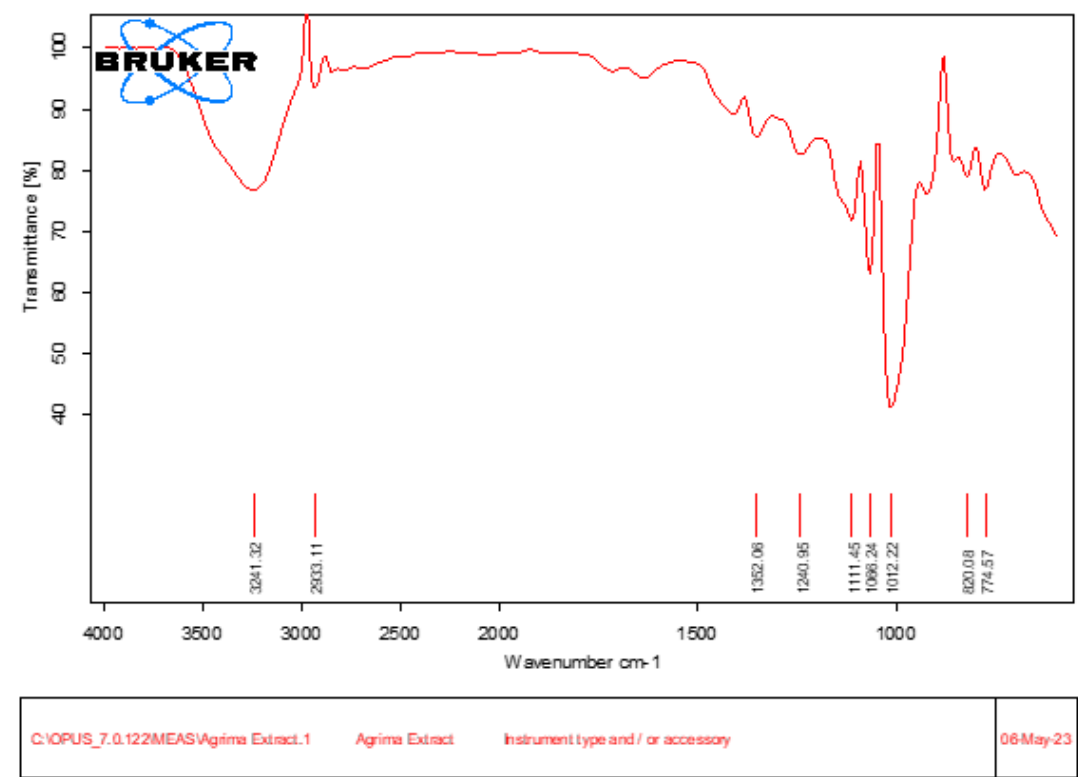


Figure 6

IR of Ethanolic Extract of *Physalis Peruviana*

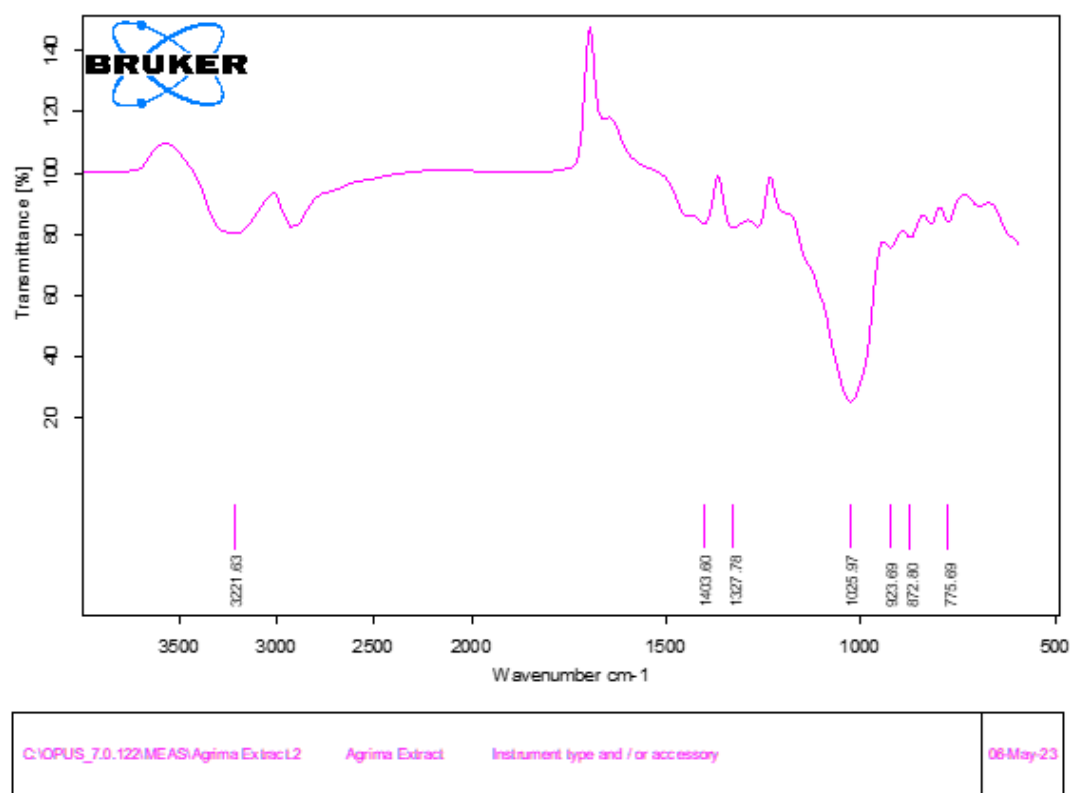


Figure 7

IR of Acetone and Water Extract of *Physalis Peruviana*

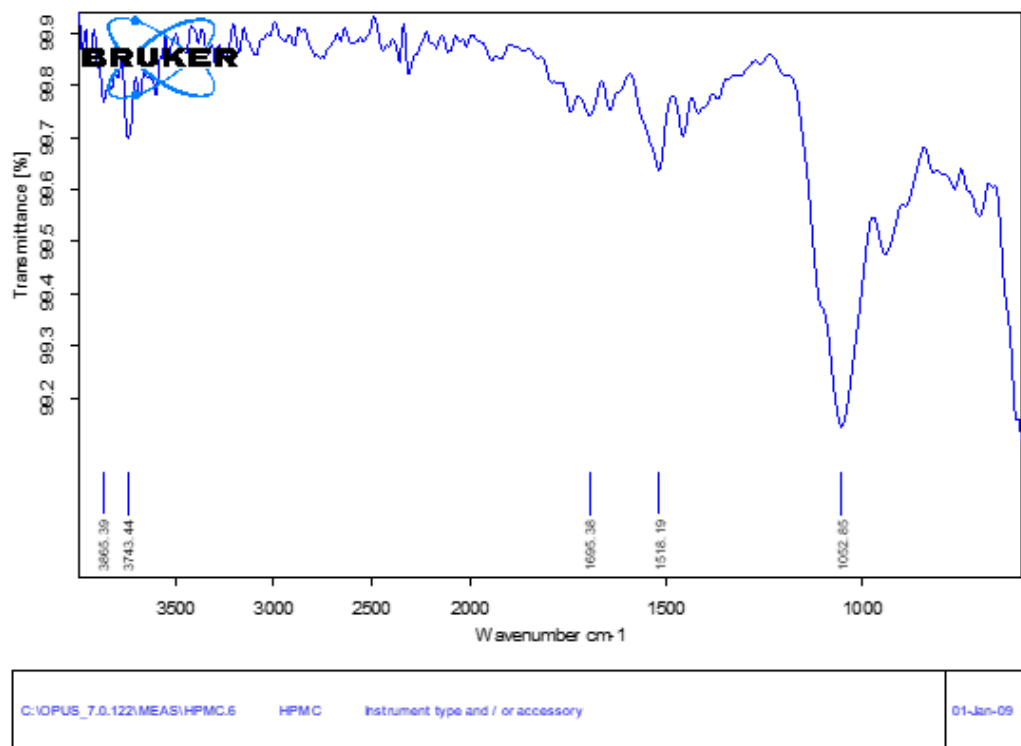


Figure 8

IR of HPMC (Hydroxypropyl Methyl Cellulose)

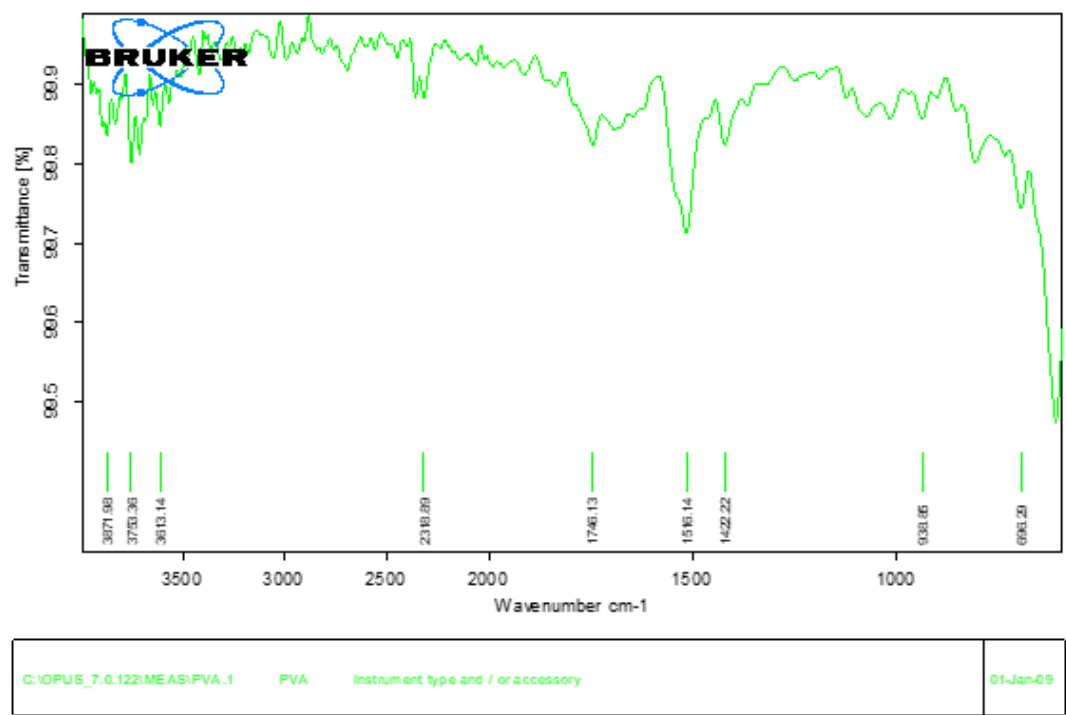


Figure 9

IR of PVA (Poly Vinyl Alcohol)

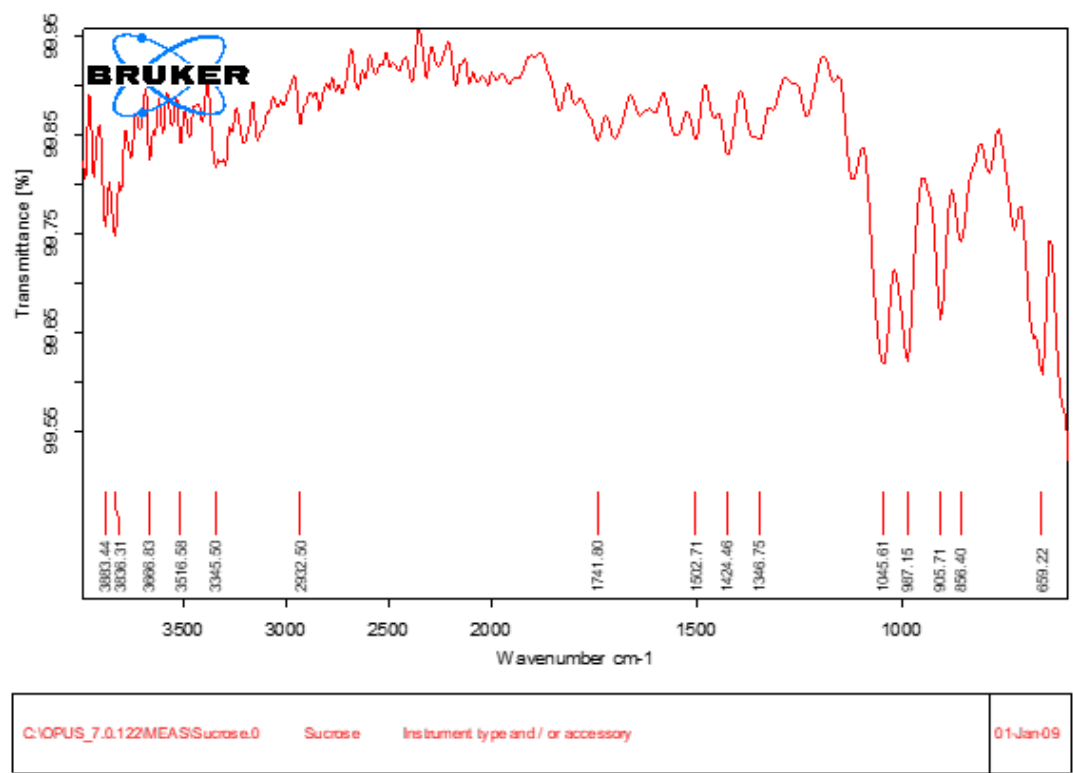


Figure 10

IR of Sucrose

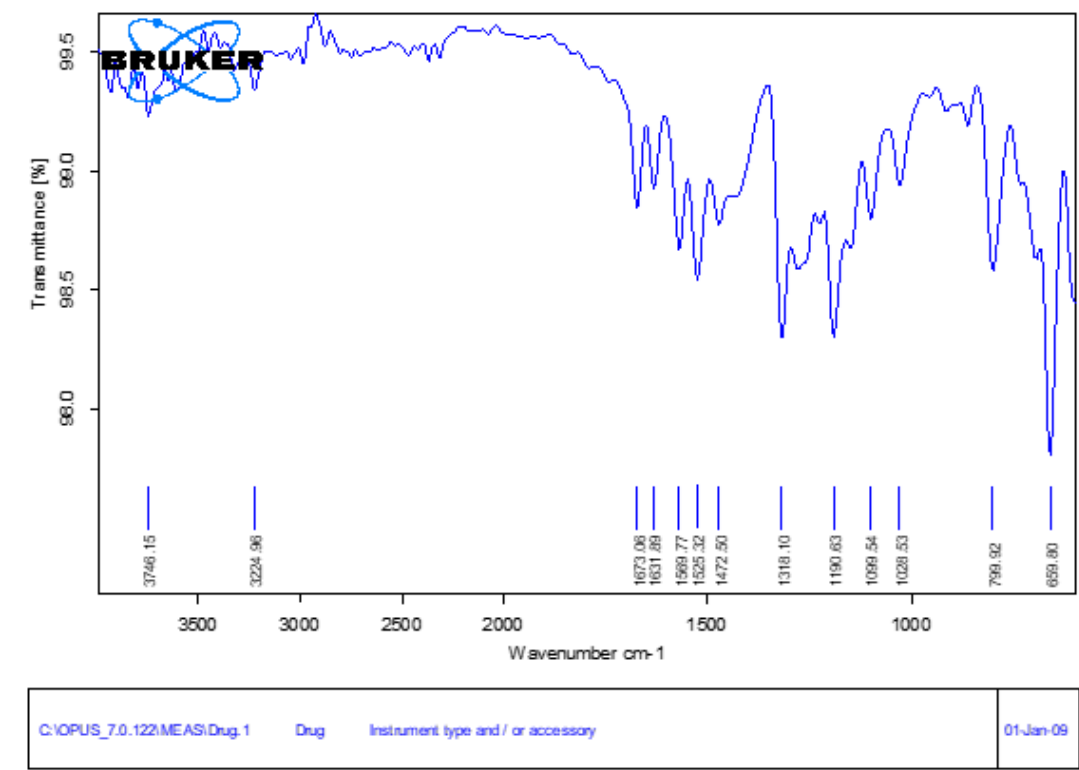


Figure 11

IR of Drug

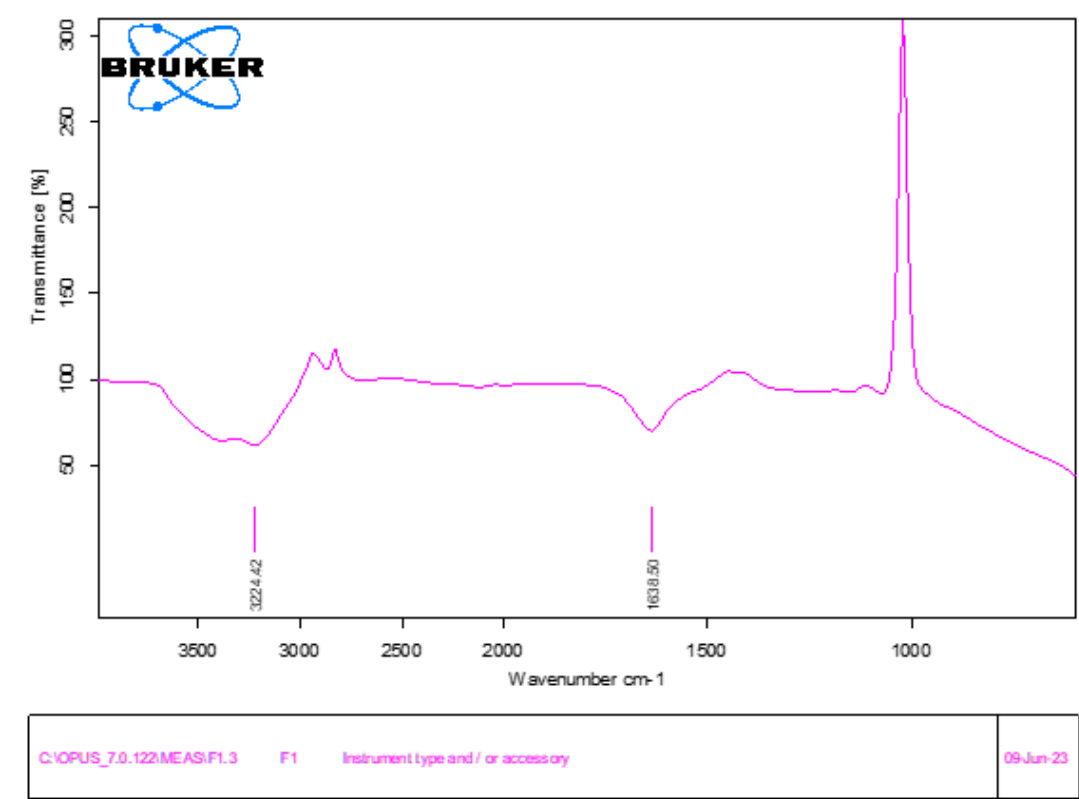


Figure 12

IR of Formulation batch of Extract

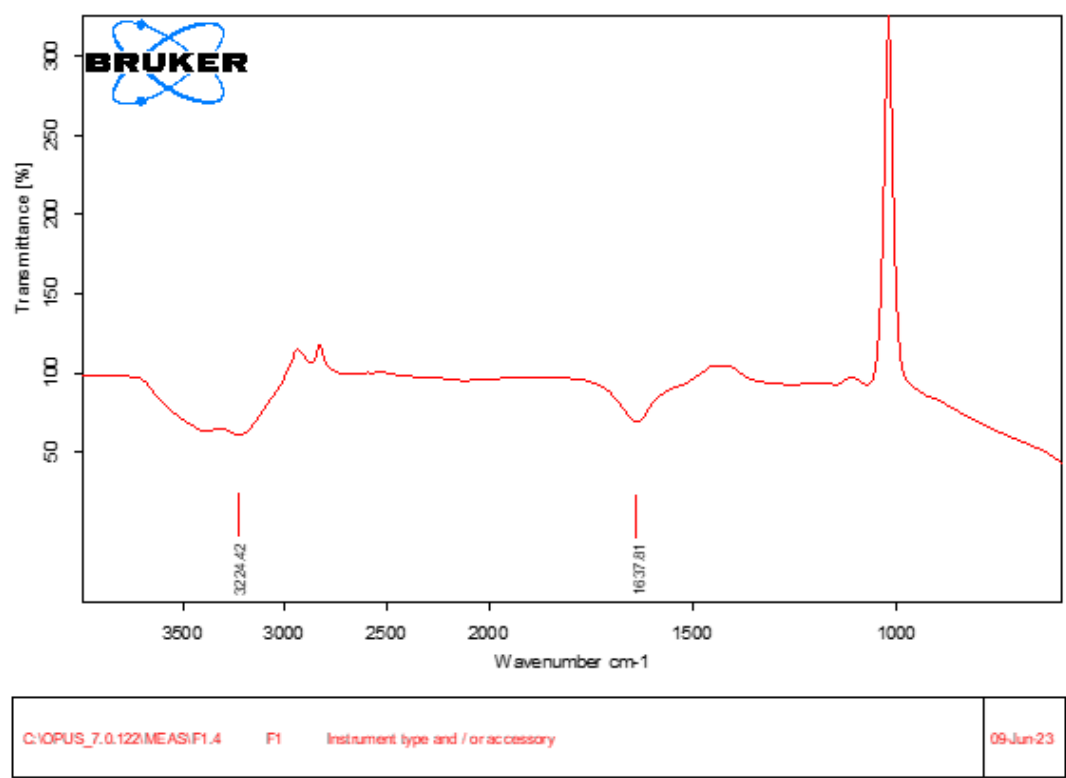


Figure 13

IR of Formulation Batch of Drug (F11)

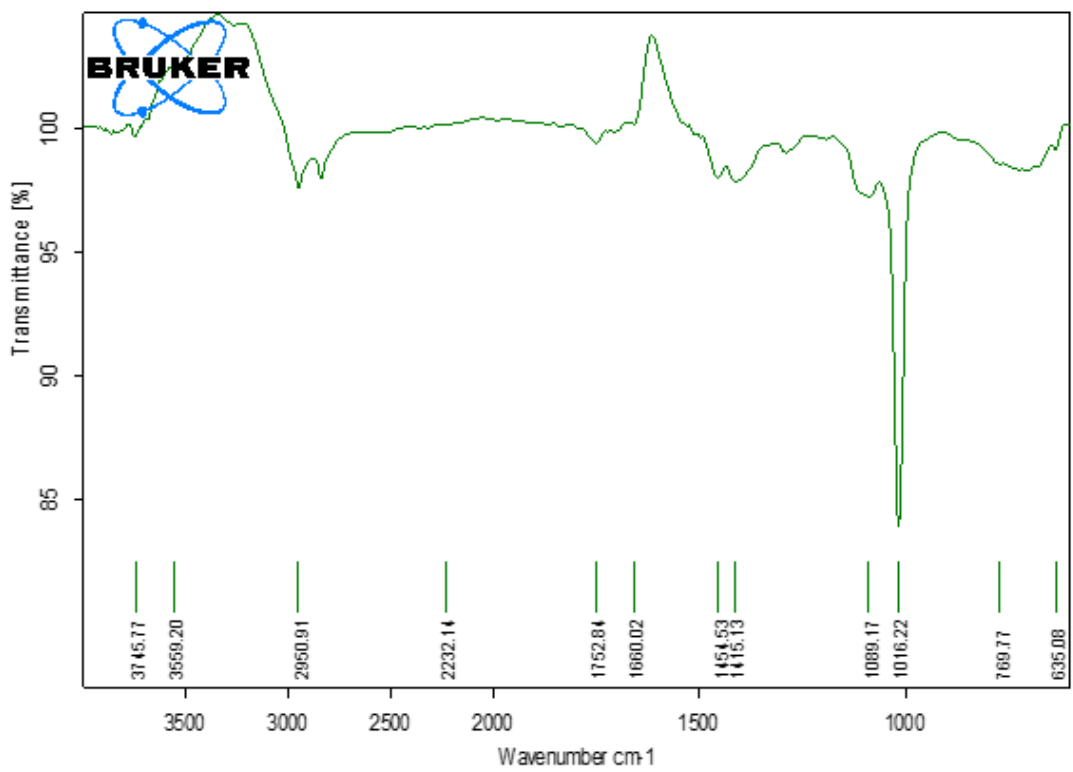


Figure 14

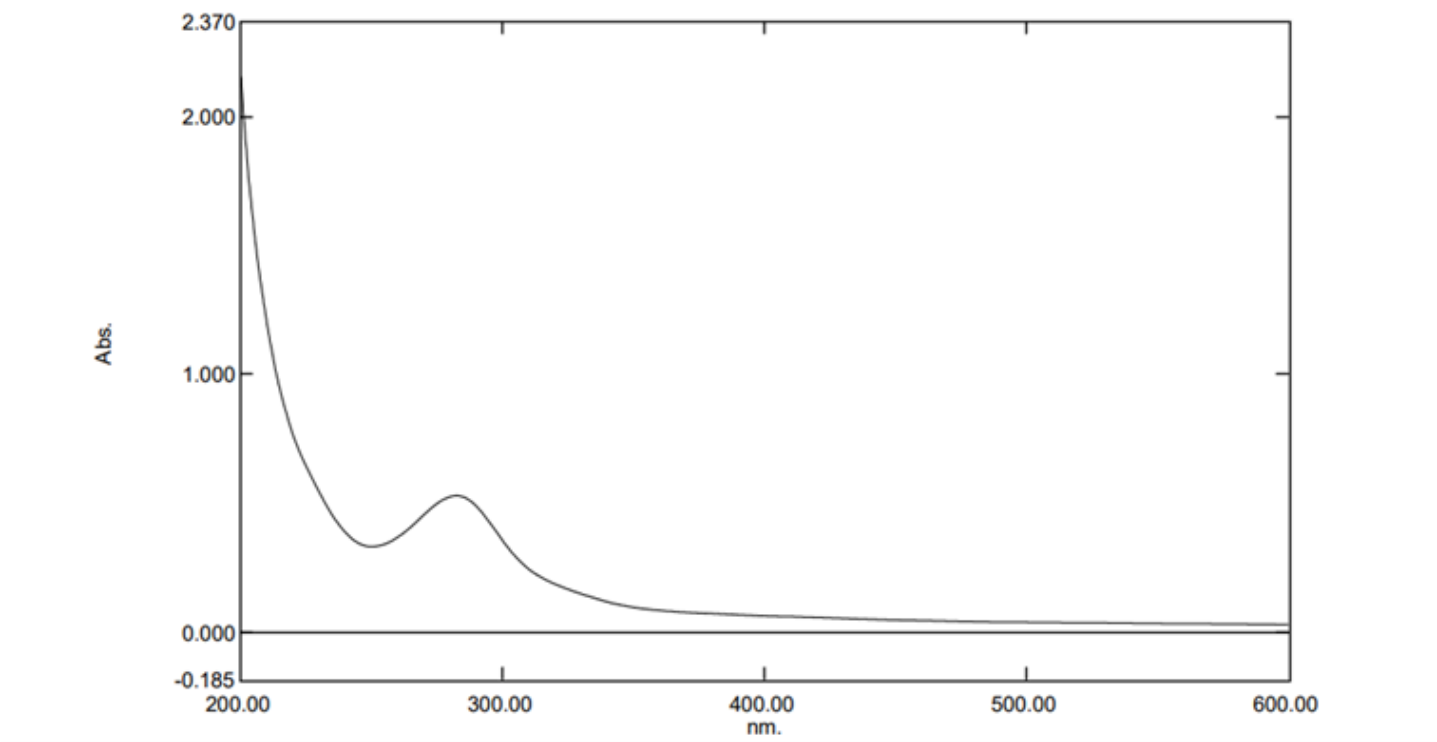


Figure 15

Lamda max determination of *Physalis Peruviana*

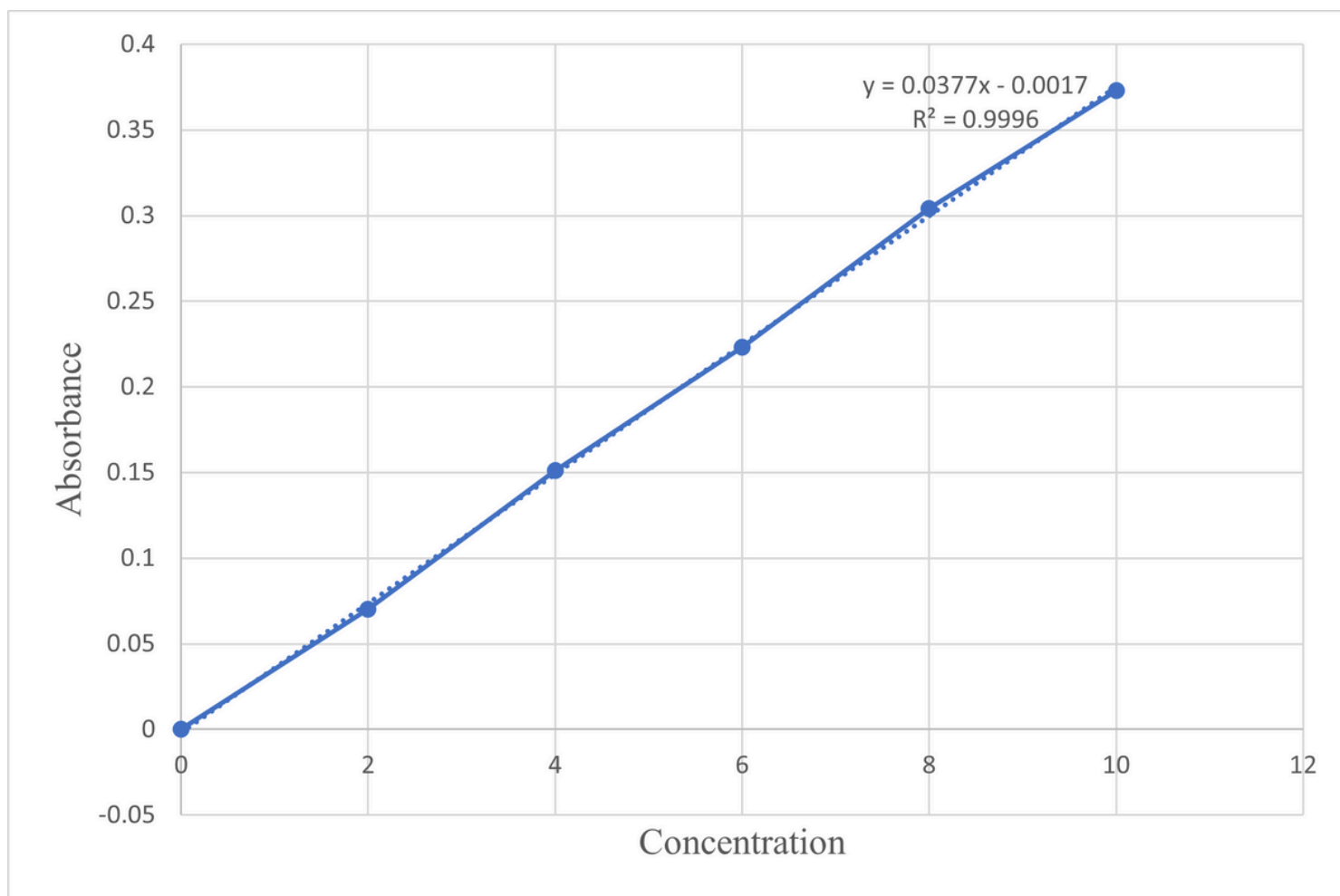


Figure 16

Physalis Peruviana extract standard curve in water

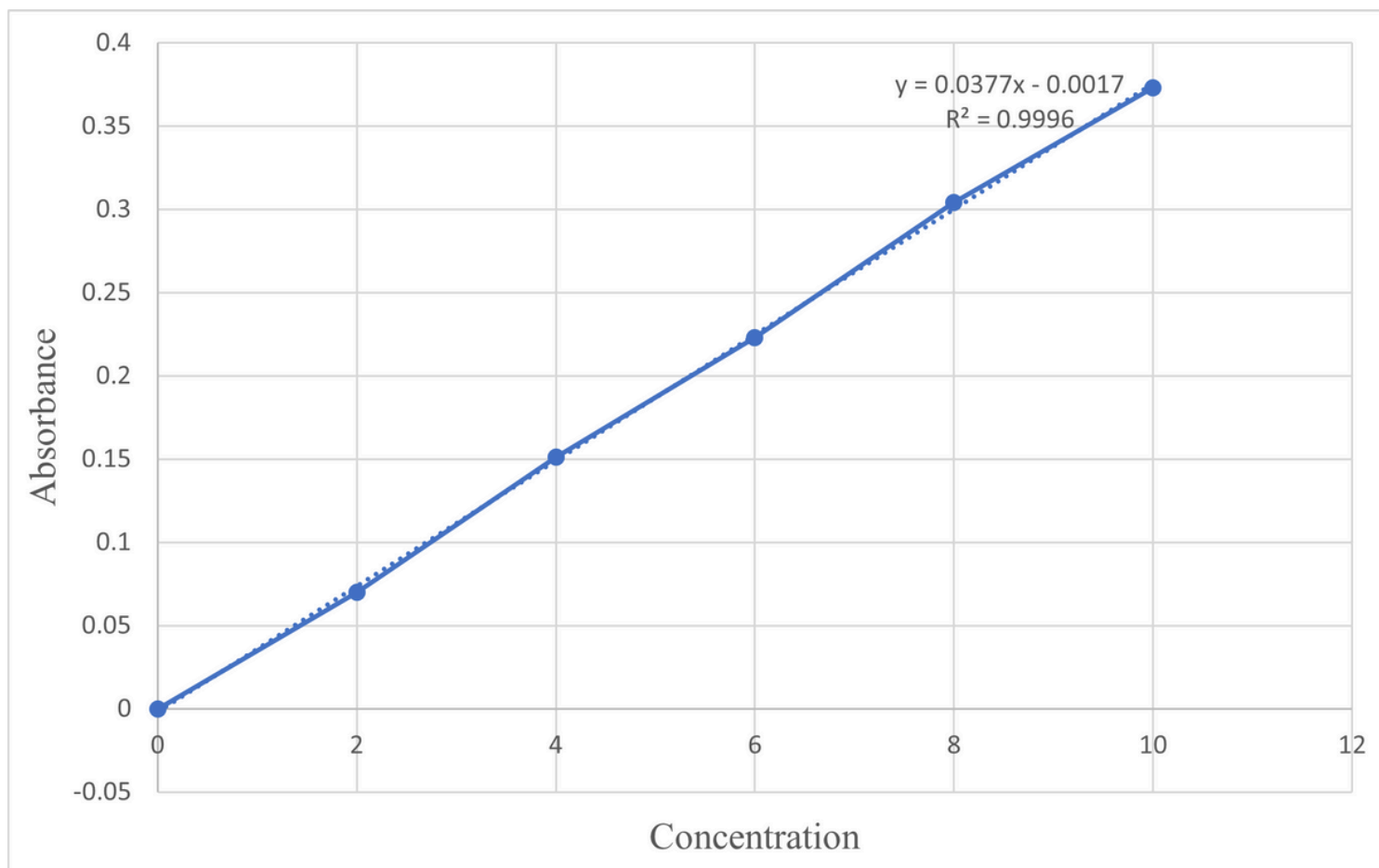


Figure 17

Physalis Peruviana extract standard curve in methanol.

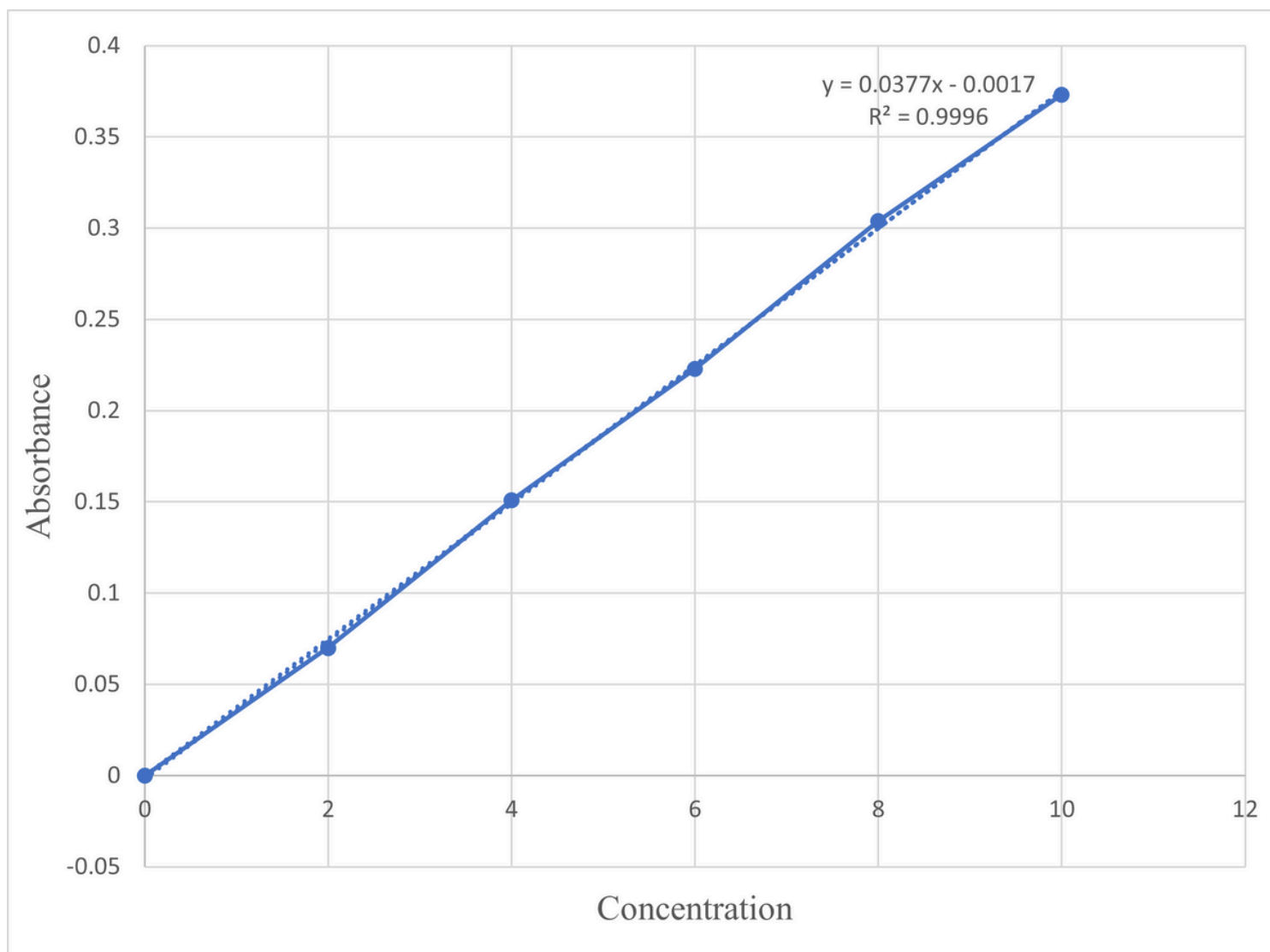


Figure 18

Physalis Peruviana extract standard curve in ethanol.

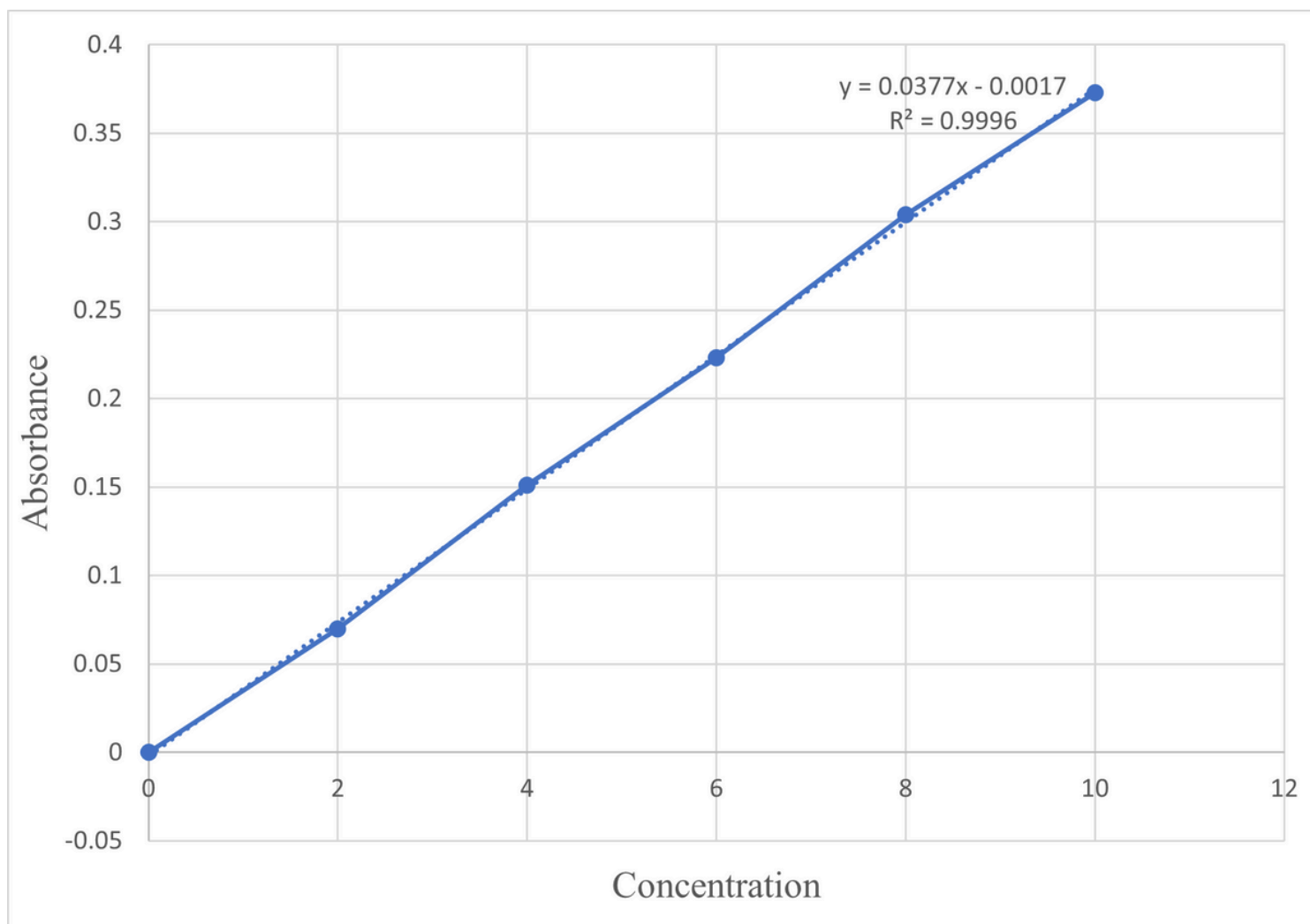


Figure 19

Physalis Peruviana extract standard curve in DMSO.

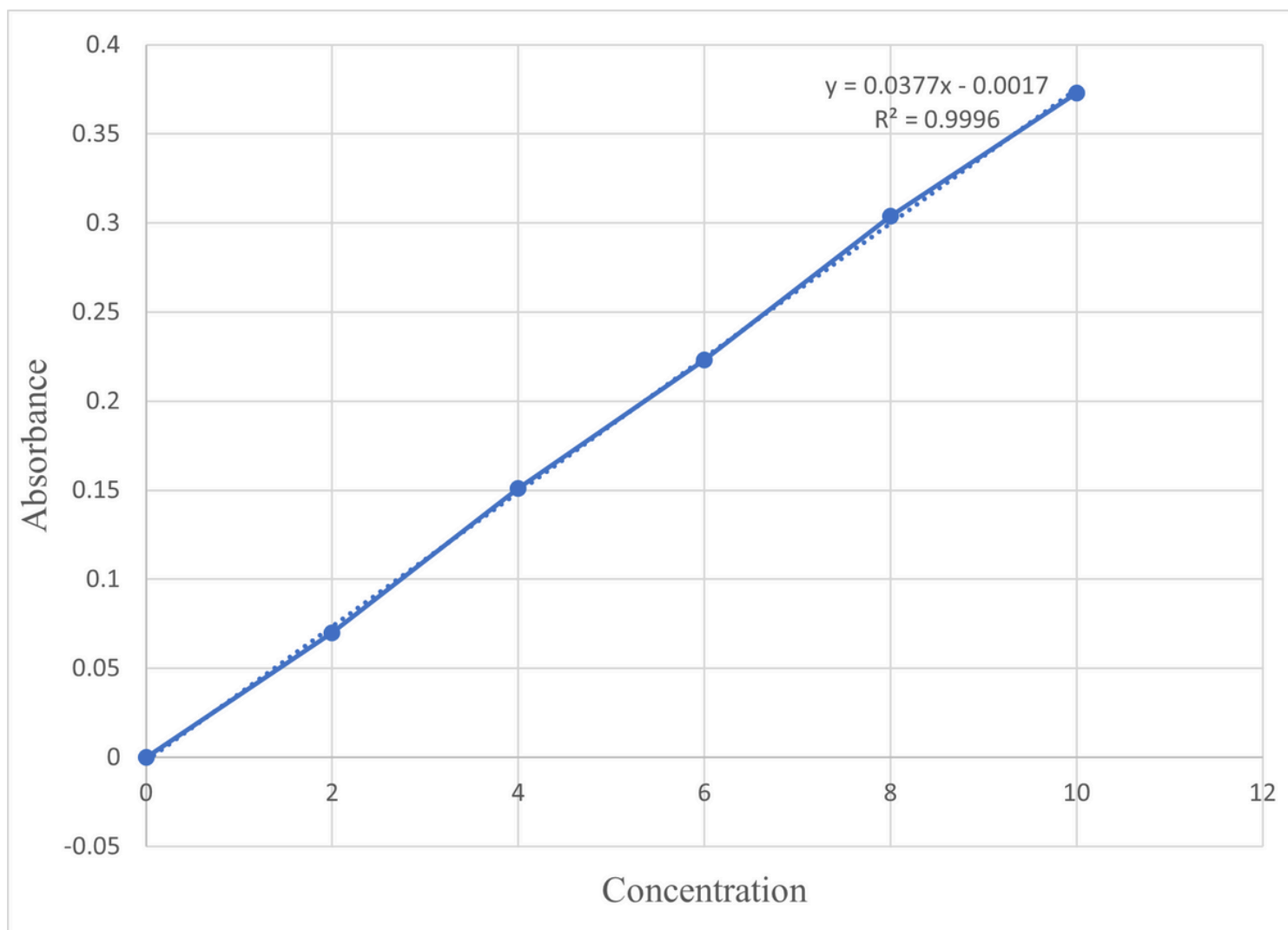


Figure 20

Physalis Peruviana extract standard curve in phosphate buffer.

Standard curve of Sunitinib Malate in Methanol

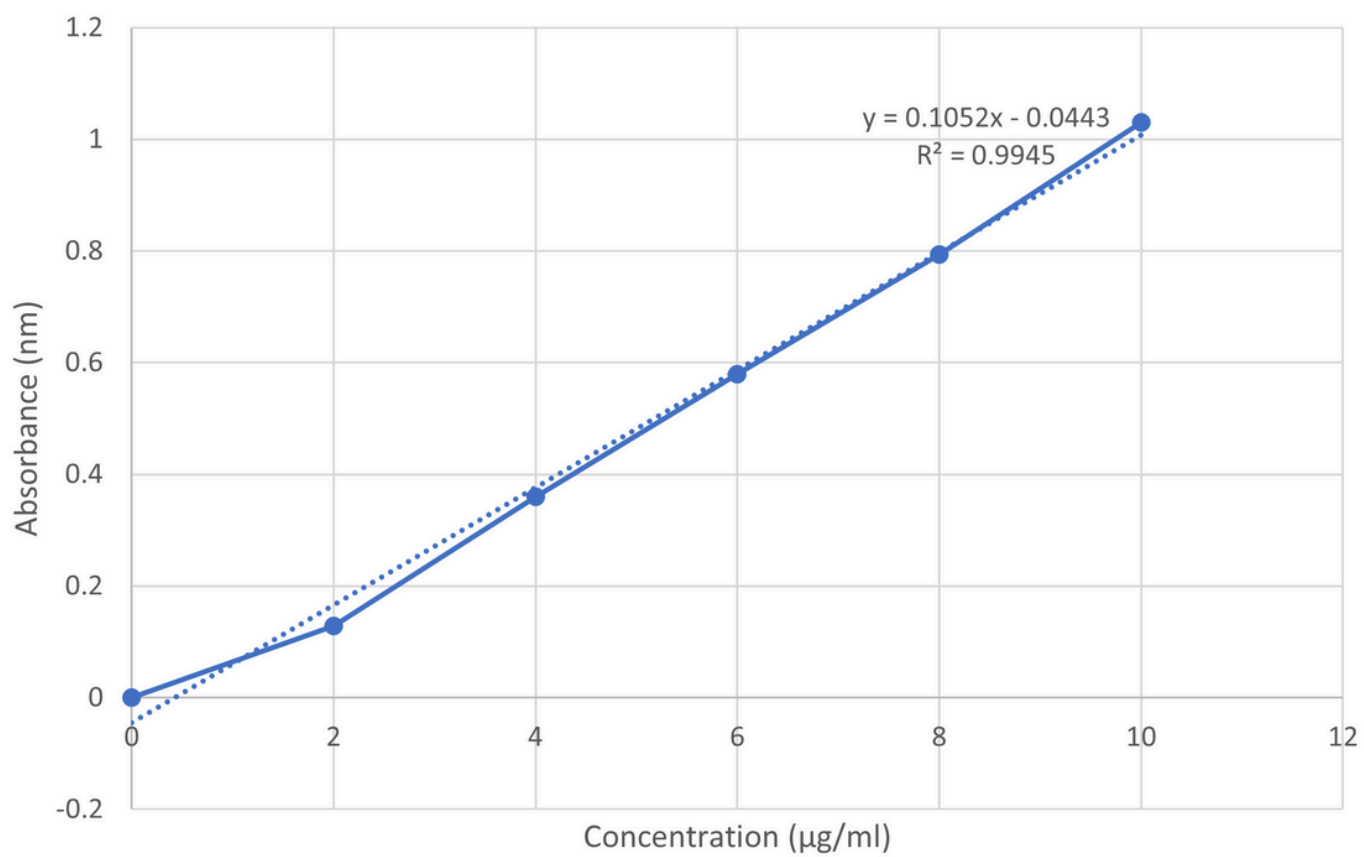


Figure 21

Sunitinib Malate standard curve in methanol.

Standard curve of Sunitinib Malate in Phosphate Buffer

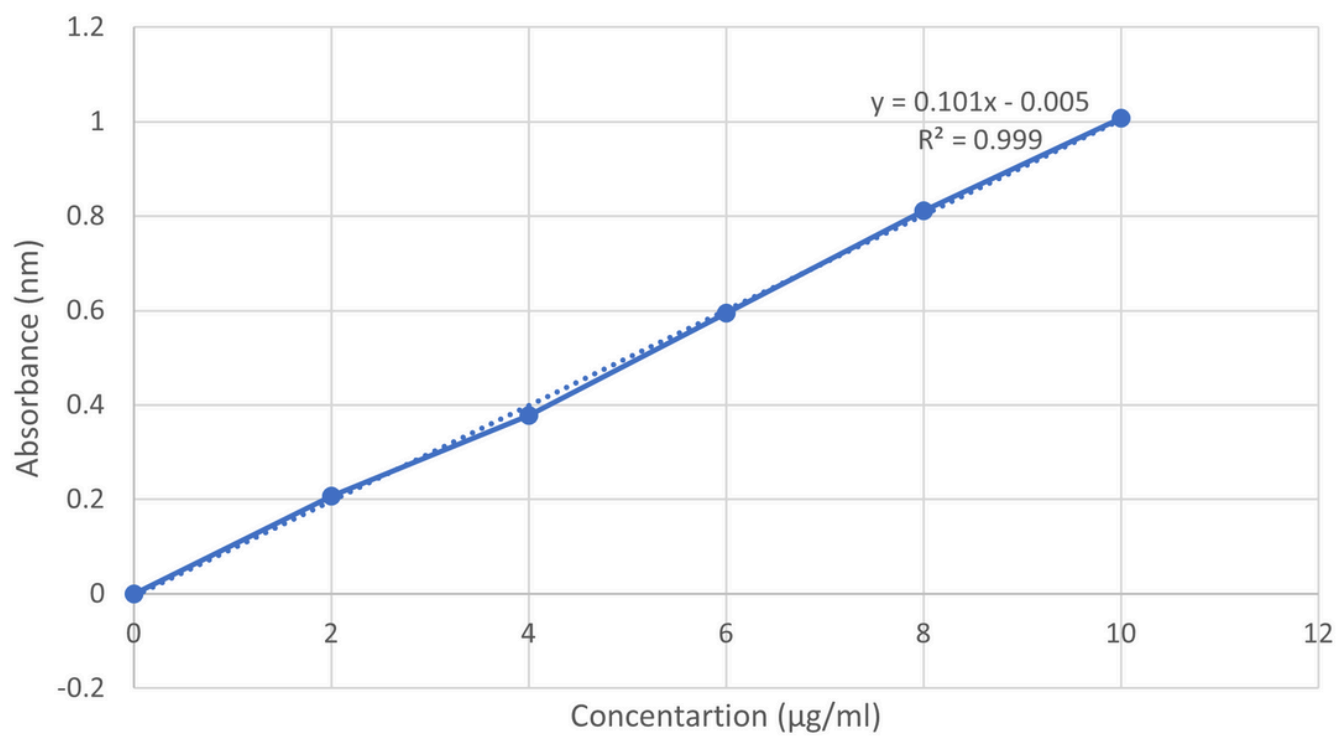


Figure 22

Standard curve of Sunitinib Malate in phosphate buffer.

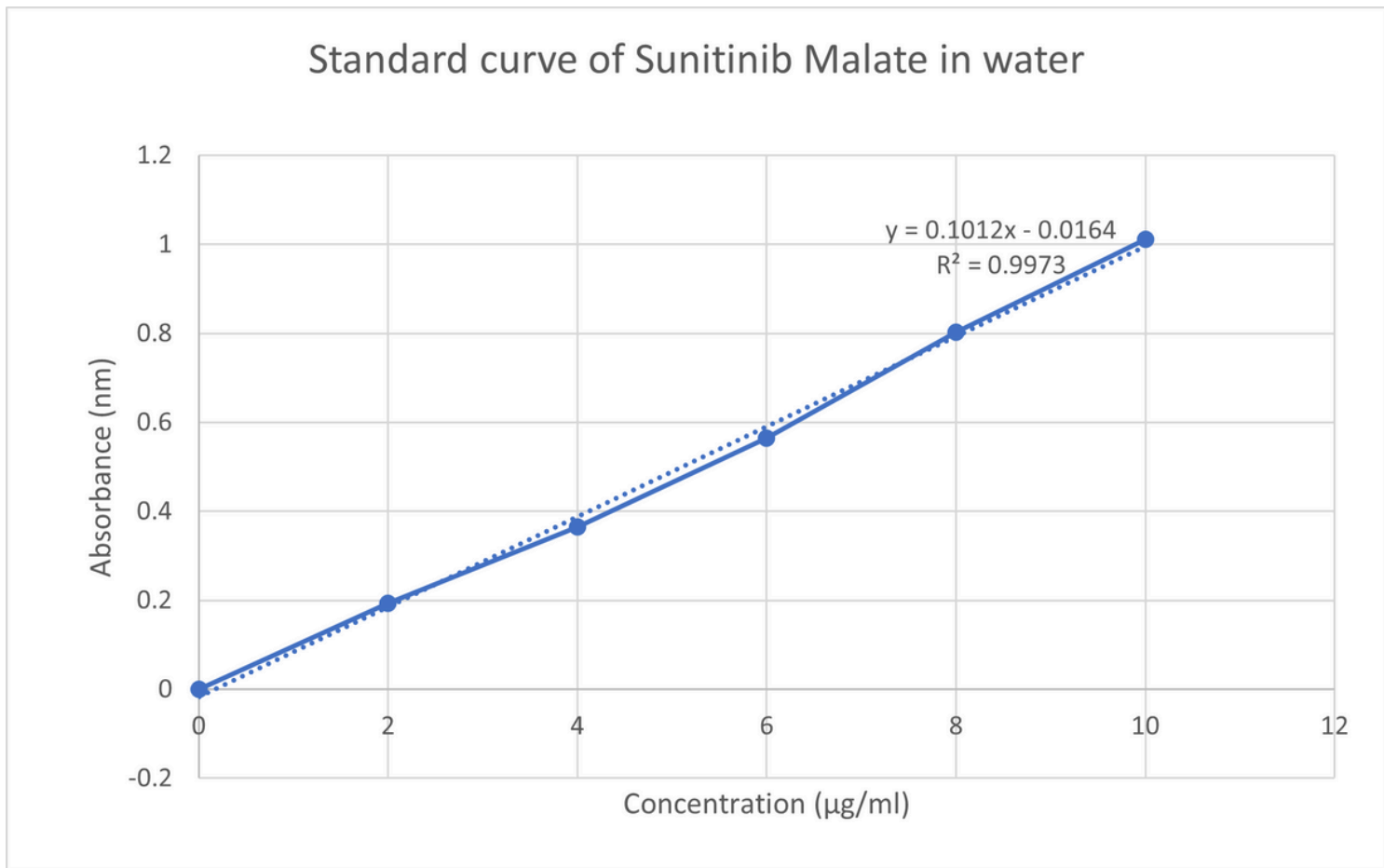


Figure 23

Standard curve of Sunitinib Malate in water.

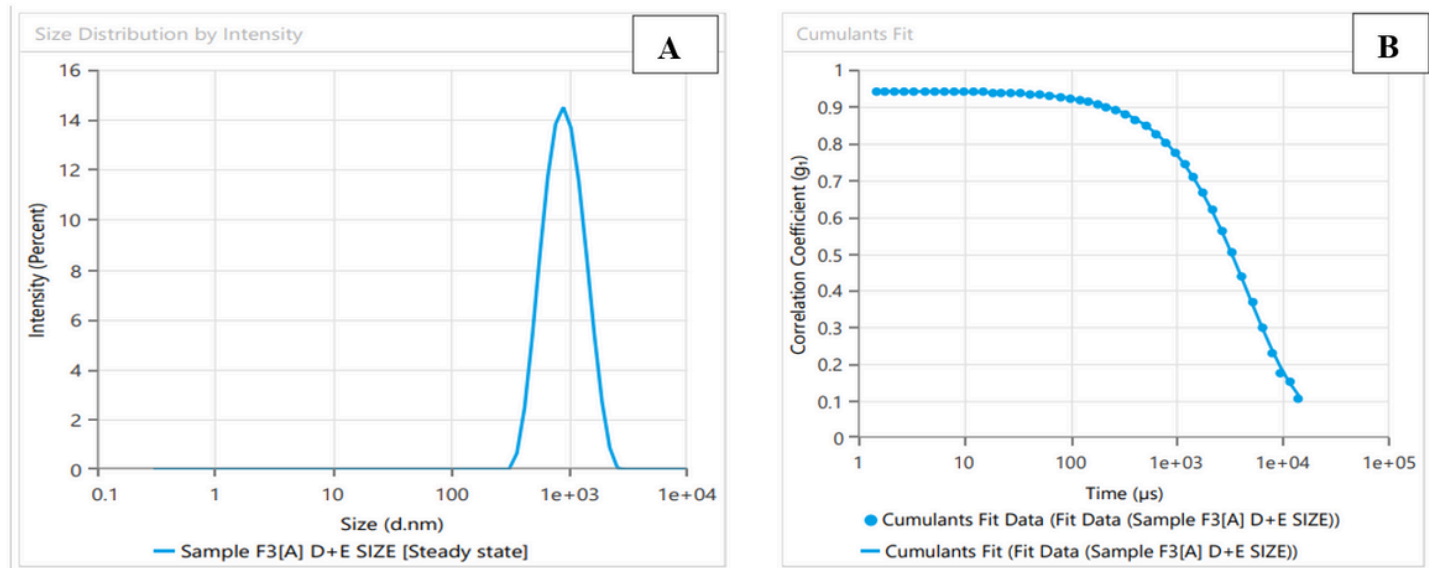


Figure 24

(A) Size distribution with respect to intensity and cumulant fit. (B) Graphical representation of batch F13.

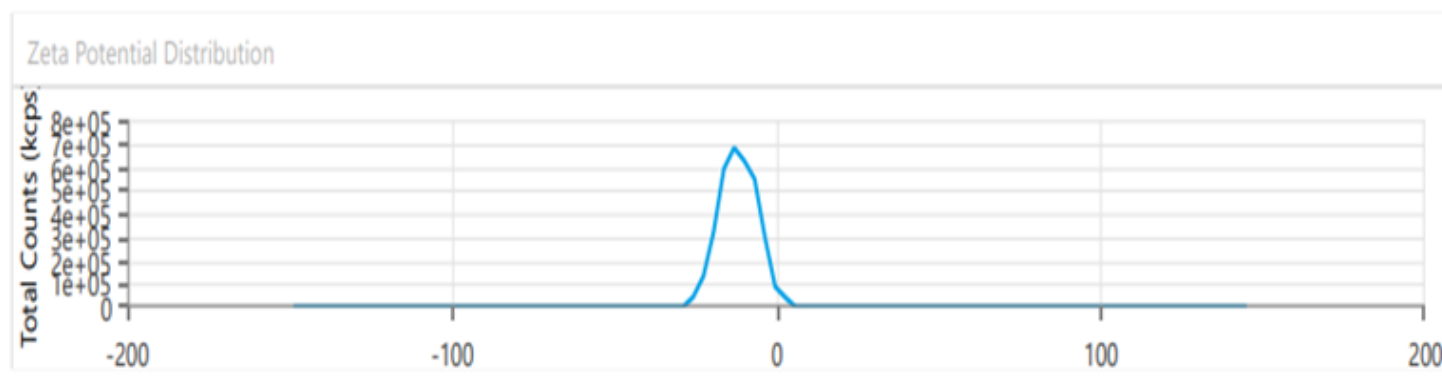


Figure 25

Zeta Potential of the formulated batch (F13)

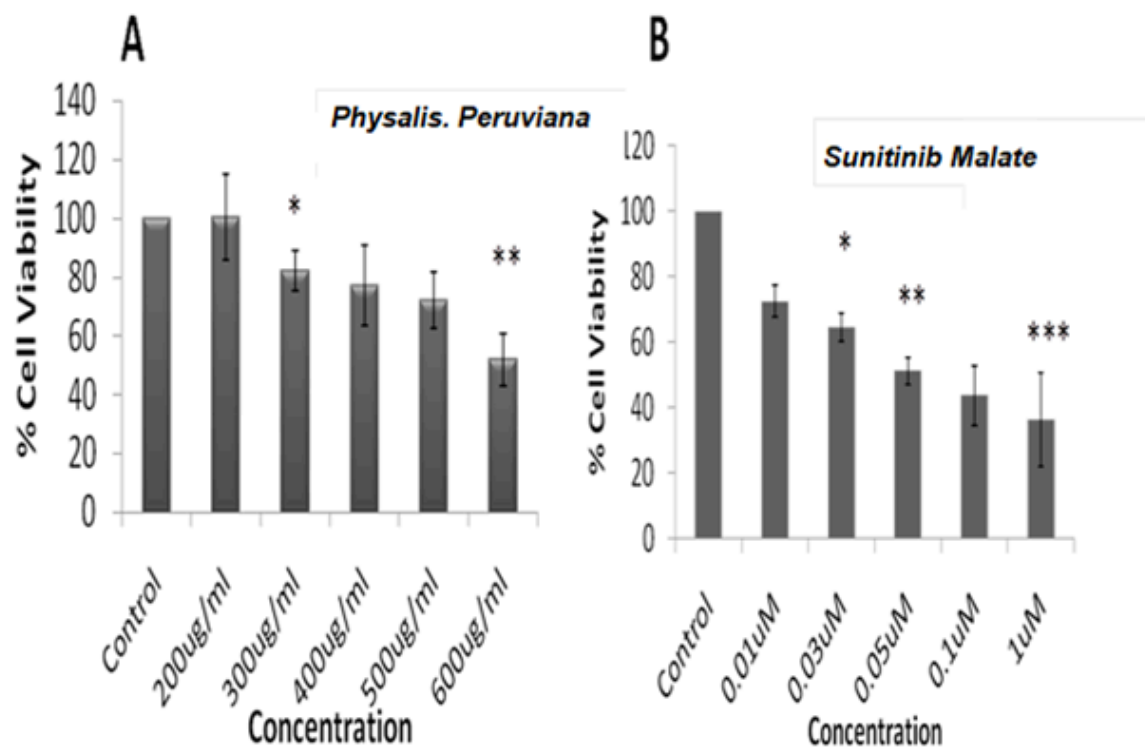


Figure 26

The Concentration of Cytotoxicity.