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SPECTRAL ANALYSIS OF NANO-PARTICLES OF TAXOL FOR INJECTABLE SUSPENSION

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ABSTARCT:

Aim In this formulation of Nano-particles to develop injectable suspension of Paclitaxel (Taxol).and paclitaxel nanoparticles prepared by precipitation techniques and the FTIR analysis and in vitro drug release, zeta potential and stability study were evaluated. Result that these studies provided conceptual proof that the nanoparticles size is (635-717nm) and the formulation PXN-6 were showed the good result for all the evaluation parameters.

Key words: Taxol, nanoparticles, Suspension, FTIR

INTRODUCTION: The first time paclitaxel (PX) was found, it was isolated from the bark of the Pacific Yew (Taxusbrevifolia). Paclitaxel is a white, crystalline powder with a melting point of about 210°C. It is one of the most successful chemotherapeutic medications and is mostly used to treat cancers of the breast, ovary, and lung, among others. PX works by promoting and stabilizing microtubules while blocking the late G2 or M stages of the cell cycle, which results in cell death. Since PX's limited water solubility (0.4 g/mL) is one of its main drawbacks, it is manufactured under the trade name "Taxol" in organic solvents made of Polyoxyethylated castor oil (Cremophor EL) and dehydrated ethanol (50/50, v/v).[1]

Recent years have seen a rise in interest in nanoparticle delivery systems, particularly for cancer treatments. PX is a potent chemotherapeutic drug that has been developed in a number of nano-delivery systems with a number of benefits over conventional therapy. First, when PX is conjugated with water-soluble polymers or enclosed in lipid-based NPs, its aqueous solubility can be significantly increased. Second, because to the enhanced permeability and retention (EPR) effect, they can be delivered preferentially into the tumour site due to their small size (a few to several hundred nanometers in diameter). Thirdly, they are able to avoid the reticuloendothelial system (RES) in healthy tissues, which lessens the adverse effects of the medication.[1]

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MATERIAL AND METHODS:

Material: The active pharmaceutical ingredients (Paclitaxel) was collected from the sun pharma as a gift sample for this project. And Silver Nitrate, Tripoly Citrate (TPP), Methanol Acetone, Dichloromethane, Isopropyl alcohol, l N-hexane, Butyl 4- Amino, benzoate (Butamben), Starch Hydroxy propyl Methyl cellulose these all chemicals are collected from the N.S scientific Ltd. Bhopal.

FTIR Spectral analysis:

In order to determine whether the chemical makeup of the medicine changed after being combined with the polymers, FTIR spectral analysis of pure drug and polymers was conducted. A little over 2 mg of the samples were combined with an equivalent amount of potassium bromide, then crushed to form pellets under pressure of 600 Kg/cm2, which were then scanned with an IR equipment (Shimadzu, 8400 Series, Tokyo, Japan) between 400 and 4000cm-1.[3]

Calibration curve :

The calibration curve for paclitaxel was prepared by using phosphate buffer (pH 7.4).

Phosphate buffer pH 7.4:

In order to make phosphate buffer, 25ml of 0.2M potassium hydrogen orthophosphate solution and 19.55ml of 0.2N sodium hydroxide solution were combined in a 100ml volumetric flask, and the remaining volume was filled with distilled water to the specified level. 7.4 0.1 was discovered to be the pH.

Primary stock solution for paclitaxel with phosphate buffer (pH 7.4):

Accurately weighed 100mg of paclitaxel was dissolved in 10ml of methanol in a 100ml of volumetric flask and volume was made up to the mark with pH 7.4 buffer to get a concentration of 1000µg/ml.

Secondary stock solution for phosphate buffer (pH 7.4):

From primary stock solutions of phosphate buffer 10ml was pipetted out in a 100ml of volumetric flask and volume was made up to the mark with pH 7.4 buffer to obtain a concentration of 100µg/ml.

From secondary stock solutions, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5 and 5.0ml were piped out and diluted to 10ml with respect buffers to get a concentration range from 5µg/ml to 50µg/ml. Then it was analyzedspectrometrically at 220nm. The calibration curve was plotted with the absorbance Vs concentration (µg/ml).

Method of preparation for Paclitaxel silver nitrate Nanoparticles by precipitation Technique: Silver nitrate and trisodium citrate were used as starting materials for the preparation of Paclitaxel silver nitrate Nanoparticles (NP). The silver colloid was prepared by using chemical Precipitation method. All solutions of reacting materials

were prepared in distilled water. In typical experiment 50 ml of 0.001 M AgNO3 was heated to boil. To this solution 5 mL of Paclitaxel (150 mg/5 ml of methanol) solution was added followed by addition of 5 ml of 1 % of trisodium citrate added drop by drop. During the process, solutions were mixed vigorously and heated until change of color was evident (pale yellow). Then it was removed from the heating device and stirred until cooled to room temperature. The colloidal solution of silver Nanoparticles were characterized by using UV-Visible spectroscopy and SEM. The entire addition process took about 3 minutes, after which the stirring was stopped and the stir bar was removed. Reaction conditions including stirring time and relative quantities of reagents (both the absolute number of moles of each reactant as well as their relative molarities) must be carefully controlled to obtain stable yellow colloidal silver. If stirring was continued once all of the silver nitrate was added, aggregation began as the yellow solution first turned to darker yellow then violet and eventually grayish after which the colloid broke down and particle settled out.

In-vitro Drug Release Studies:

By using a dialysis membrane with a pore size of 2.4 mm (LA-395-5Mt HimediaPvt. Ltd, Mumbai, India) and 75 ml of pH 7.4 phosphate buffer at 37°C, Paclitaxel Silver Nitrate Nanoparticles were released in vitro. 75 ml of phosphate buffer with a pH of 7.4 were taken quickly into a 100 ml beaker. The buffer solution was added to a dialysis bag containing 2 ml of the formulation. The dialysis membrane was previously activated by soaking in 1% w/v NaOH for an overnight period. A magnetic stirrer was used to keep the flask in place. The buffer was kept at a constant temperature of 37°C while stirring was kept at 250 rpm. Sampling was carried out by taking 1 ml aliquots out of a beaker. To maintain the sink condition, 1 cc of fresh buffer was introduced right away. Samples were examined using a UV/Spectrophotometer (UV/VIS-Double beam Spectrophotometer, V-530, Jasco, Tokyo, Japan) at a wavelength of 271 nm after being adequately diluted with methanol. Each test was carried out three times, with the average value used in the calculation.

Application in first order release:

Several different types of modified release pharmaceutical dosage forms, such as some transdermal systems, matrix tablets with low solubility medicines in coated forms, osmotic systems, etc., can all be described by this relationship.[5,6]

The release of the drug which followed first order kinetics can be expressed by the equation:

$$\mathbf{dc/\ dt = -Kc\ (1)}$$

Where K is first order rate constant expressed in units of time^{-1}.

Equation (1) can be expressed as:

$$\mathbf{\log C = \log C0 - Kt\ /\ 2.303\ (2)}$$

Where k is the first order rate constant, t is the time, and C0 is the starting drug concentration. The data are plotted as log cumulative percentage of medicine remaining vs. time, which results in a line with a slope of -K/2.303 and a straight shape.

Application in Higuchi release equation:

This relationship can be used to explain the drug dissolution in pharmaceutical dosage forms such as those containing water-soluble drugs in permeable matrices.[7,8]

The Higuchi release equation is:

$$Q = KHt^{1/2}$$

Where Q is the cumulative amount of drug release at time "t" KH is Higuchi constant, T is time in hours.

The Higuchi equation suggests that drug release by diffusion.

When the cumulative percentage of medication release is shown on the y-axis and the square root of the time required on the x-axis, a straight line results.

Zeta Potential Analysis:

The zeta potential was measured using the appropriate instrument (Beckman Coulter Delsa Nano C, Brea, USA).using automatic titration regime that adjusts the pH of the sample to pre-defined values by adding 0.1M HCL or 0.1M NaOHtitrator a volume of 20 ml suspension is necessary.[4]

Stability studies:

The goal of stability testing is to provide proof of how the quality of the drug substance or product changes over time under the influence of various environmental factors, such as temperature, humidity, and light, in order to determine a shelf life and

recommended storage conditions for the drug substance or product. The capacity of a certain formulation, in a specific container, to remain within its physical, chemical, pharmacological, and toxilogical requirements is referred to as drug stability.

Accelerated stability experiments on the batch-optimized paclitaxel silver Nitarte nanoparticles were conducted. The 150 mg Paclitaxel Nanocapsule from the PXN6 batch was put into a size 1 capsule. In order to create the capsule's total weight of 290 mg (161+129), lactose was utilized as a diluent.The samples were examined after 0, 1, and 2 months. The data was examined for any appreciable deviations from the starting point. The subsequent tests were run:

1. Test for physical parameters 2.Assay 3.In-vitro dissolution study.

Result:

FT-IR spectral analysis:

Calibration Curve:

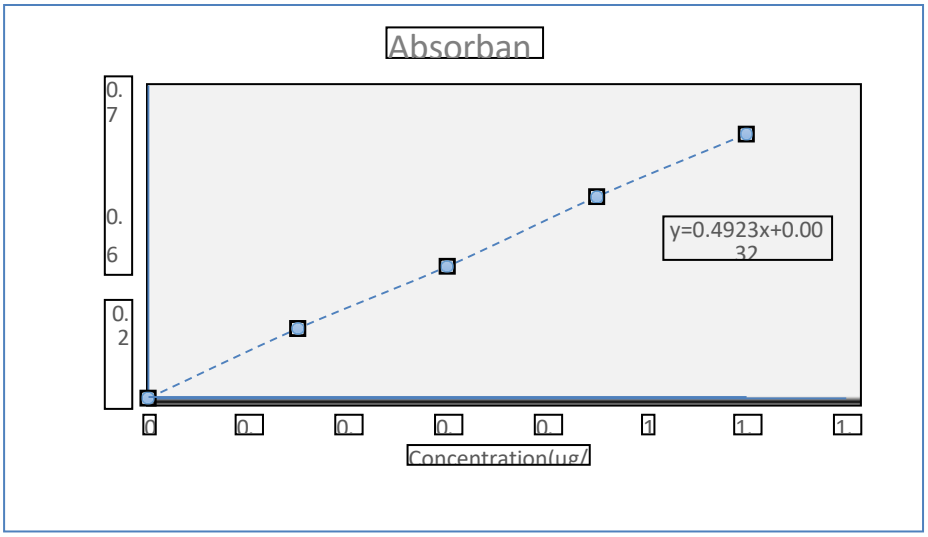

Fig1. FTIR Spectrum of Formulation paclitaxel

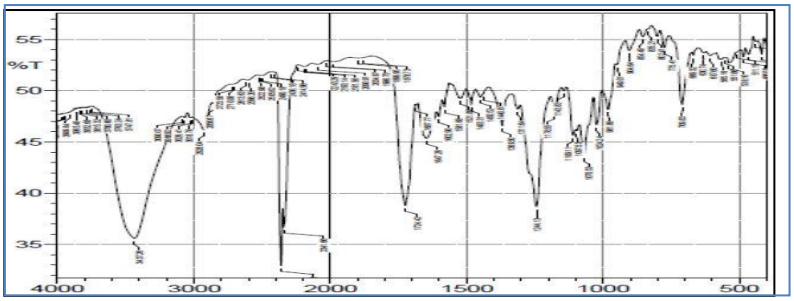

Fig2. Calibration curve of paclitaxel in pH 7.4 at 220nm

In-vitro Drug Release Studies:

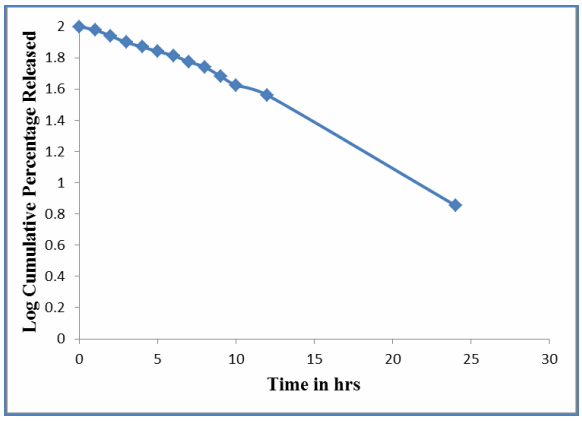

Fig3. ZeroorderReleasePlotforFormulationPXN-6

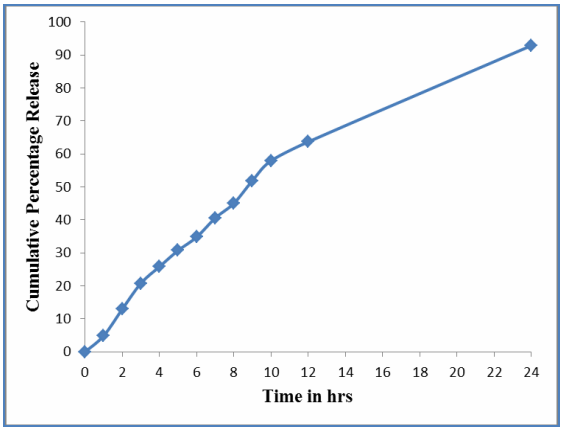

Fig4.FirstorderReleasePlotforFormulationPXN-6

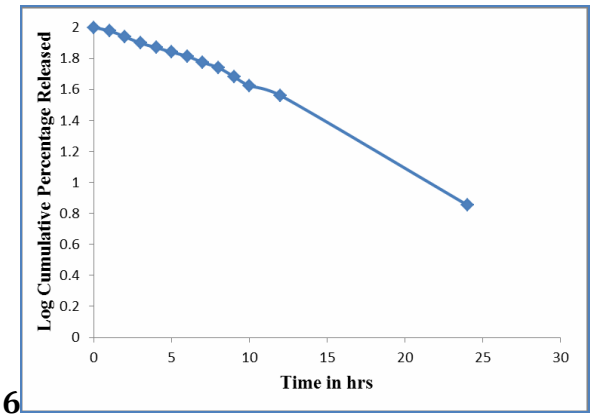

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Fig5. Higuchis Release Plotfor Formulation PXN-

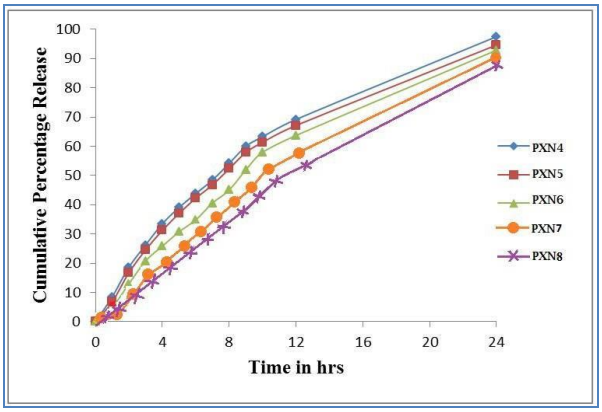

Fig6: Comparative Zero order Release Plot for

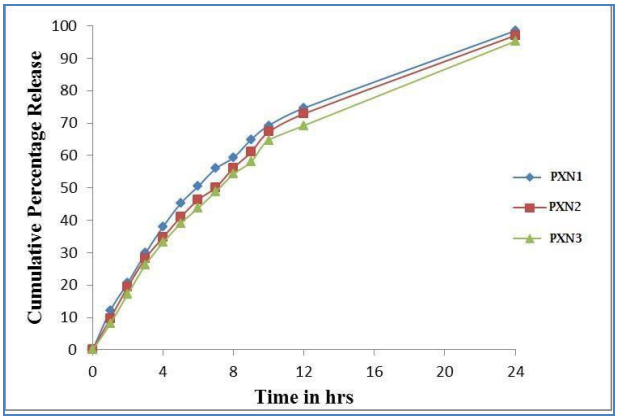

Fig7: Comparative Zero order Release Plot for

Formulations PXN-1 to PXN-3 Nanoparticles

Formulations PXN- to PXN- Nanoparticles

Zeta Potential Analysis:

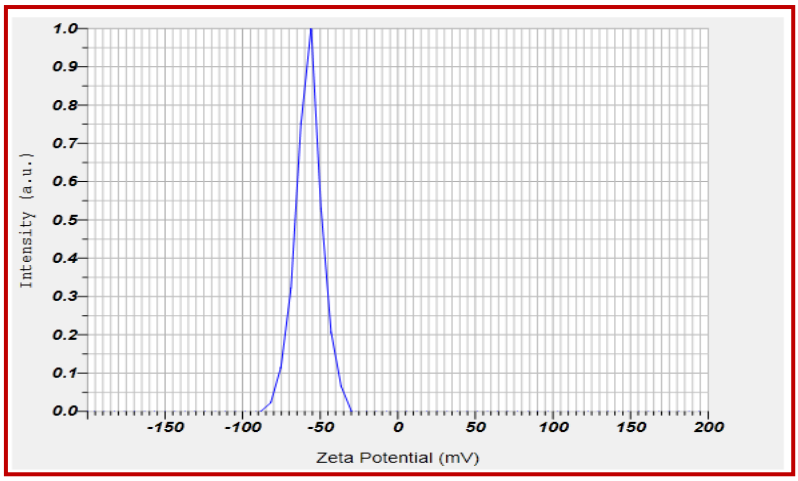

Fig8. Zeta potential Analysis of Paclitaxel silver nitrate nanoparticles

Stability Studies:

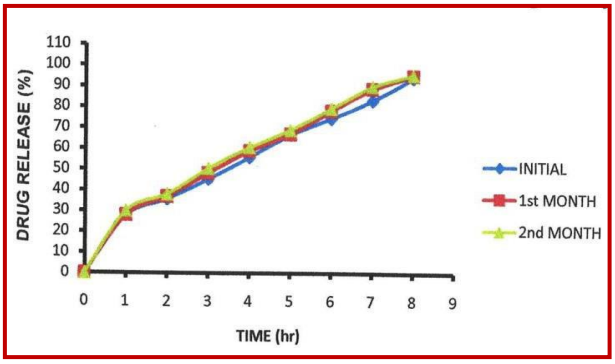

Fig9: Comparative dissolution profile of Paclitaxel silver nitrate Nanoparticles (stability study)

Discussion:

The choice of Paclitaxel was influenced by its cost-effectiveness, ease of availability, and challenging pharmacological characteristics during the formulation development process. Paclitaxel silver nitrate nanoparticles were made using trisodium citrate and silver nitrate as starting ingredients. Chemical precipitation was used to create the silver colloid. This resulted from numerous trial batches. The Paclitaxel Nanoparticle formulation was finally completed. And Further test or evaluation done for the Nanoparticle.

Conclusion:

The results of the current in vitro investigation showed that Paclitaxel NP may be a suitable drug delivery method for the colon. 60% of the medicine will be released at the colon following a typical GIT (Gastrointestinal Tract) of 4-6 hours. This research reveals that paclitaxel NP solutions with sizes between 635 and 717 nm are stable at neutral ph.

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