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FORMULATION AND EVALUATION OF CREAM INTEGRATING CHAMOMILE-ENHANCED MAGNESIUM OXIDE NANOPARTICLES

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***Abstract*:** The synthesis of metal oxide nanoparticles using plant extracts represents an environmentally friendly and sustainable alternative to traditional chemical methods. In particular, the use of chamomile aqueous extract for the synthesis of magnesium oxide (MgO) nanoparticles offers a green and non-toxic approach, leveraging the natural reducing properties of many hydrophilic components like flavonoids, phenyl carbonic acids etc. The biologically synthesized MgO nanoparticles were characterized using UV–Visible spectroscopy to analyze their absorption patterns, Fourier transform infrared spectroscopy (FTIR) for analyzing the functional groups, and scanning electron microscopy (SEM) for morphological studies.

Keywords: Chamomile extract, MgO nanoparticles, FTIR, SEM analysis, Cream

I. INTRODUCTION

Nanoparticles are those exist in nanometer scale is between 1 and 100 nanometers in size (Prasad et al, 2019). Green synthesis of nanoparticles has gained extensive, reliable and eco-friendly approach towards metal and metal oxide nanomaterials (Jiale et al, 2007). It is regarded as an important tool to reduce the destructive effects associated with the traditional methods of synthesis for nanoparticles commonly used in lab or industry. This approach not only minimizes the use of hazardous chemicals but also adds value to agricultural waste, contributing to waste management and environmental protection. Plants have the potential to accumulate certain amounts of heavy metals in their diverse parts. Consequently, biosynthesis techniques employing plant extracts have gained increased consideration as a simple, efficient, cost effective (Balaprasad et al, 2005) and feasible methods as well as an excellent alternative means to conventional preparation methods for nanoparticle production (Jaspreet et al, 2018; Daisy Philip, 2010).

The diverse biomolecules like carbohydrates, proteins, coenzymes, flavonoids (Ana Maria et al, 2011) and other polyphenolic compounds exhibits exemplary potential to reduce metal salt into nanoparticles. The use of various metals like gold, silver, zinc, magnesium etc have found its importance in the synthesis of nanomaterials (Aman et al, 2019). In medicine, magnesium oxide is used to relieve heartburn and sour stomach, improve bone regeneration, antimicrobial, relax muscle tension, antitumour agent etc. Many study reported MgO for its antimicrobial property (Aniruddha et al, 2013). *Matricaria chamomilla* commonly

known as chamomile, is an annual plant that belongs to Asteraceae. Chamomile tea is popular in many parts of Europe, South America and Mexico for treating digestive disturbances, fever, insomnia and cramps. Dried chamomile, especially the flowers, contains a large amount of hydrophilic constituents such as sugars, flavonoids, mucilage, phenyl carbonic acids, amino acids, choline, and salts (Jalal et al, 2014; Janmejal et al, 2010; Hojat et al, 2021).

II. METHODOLOGY

2.1 Synthesis of MgO NPs

The procedure involves the following steps:-

a. Preparation of Chamomile extract
b. Green synthesis of Chamomile mediated Magnesium oxide Nanoparticles (MgO-NPs)

2.1.1. Preparation of Chamomile extract

Dry chamomile flower heads were crushed into coarse powder. 10gms of the powder taken with 100ml of deionised water and refluxed for 1hr. The extract was filtered through Whatmann filter paper and stored in refrigerator until further use (Kokate CK, 2005).

Fig1. a)*Matricaria chamomilla* (Chamomile) b) Aqueous Extract of Chamomile

2.1.2. Synthesis of MgO-NPs

Chamomile extract of about 30ml was added dropwise to a solution containing 150ml of 0.1M MgNO3 and then continued with 1M sodium hydroxide drop wise under constant temperature (80°C) with continuous stirring over a period of 6 hours using thermostatic magnetic stirrer. The formation of nanoparticles can be observed through change in the colour of the mixture. Further, the mixture was centrifuged at 7000rpm for 10min. Subsequently, the precipitate was washed several times with water and calcinated at 400°C (Manne et al, 2021).

2.2. Characterization of Magnesium Nanoparticles

2.2.1. UV-Visible Spectroscopy Analysis & Standard Curve determination

The determination of Lambda max of Chamomile extract was done by taking 2.5mg in 100ml distilled water as standard solution and further dilutions made upto 1mg/ml. The dilutions were scanned between 200-400nm using UV-Vis Double beam spectrophotometer. Further five dilutions were made with concentrations 0.1, 0.2, 0.3, 0.4, 0.5 mcg/ml for determination of standard curve against distilled water as blank. The analysis is carried out at UV-Vis Double Beam Spectrophotometer (Kumar Sneha et al, 2022; Cheviron et al 2014).

2.2.2. FTIR Spectral Analysis

It is a versatile tool for surface characterization of nanoparticles. FTIR is helpful in identifying structural differences in molecular binding and the reactive surface sites responsible for the surface reactivity. Dried powder as well as liquid sample of chamomile extract and MgO nanoparticles were used for FTIR analysis. KBr pellet was prepared for MgO nanoparticles using conventional method while chamomile extract and MgO nanparticle in water sample were prepared for analysis. The samples were loaded in FTIR

spectroscope (Waters, IR Affinity 1, Japan) with a scan range from 400 to 4000 cm^{-1} with a resolution of 4cm^{-1}(Asep Bayu et al, 2019).

2.2.3. Scanning Electron Microscopy

It is necessary to study the morphology of MgO nanoparticles synthesized. The SEM images of the silver nanoparticles are taken. The micrographs are recorded using JEOL-Scanning Electron Microscope (SEM), JSM-5610LV, with an accelerating voltage of 20KV, at high vacuum (HV) mode (Fayaz et al, 2010).

2.3. Cream Formulation

To prepare 50gm of W/O type MgO NPs cream, the required quantities is taken as specified in Table No.1. W/O cream was prepared as given by swetha et al with slight modification. Similar, formulation is prepared neglecting the sample and it was considered as Control cream (Swetha et al, 2023; Michael et al, 2019).

Table No.1 Formulation of Control and MgO Nanoparticles (MgO NPs) Cream

Ingredient Name	CE-MgO NPs W/O Cream (For 50gm)	Control W/O Cream (For 50gm)
Bees wax	10	10
Liquid Paraffin	30	30
Borax	0.5	0.5
Water	9.5/q.s	9.5/q.s
CE-MgO NPs	0.1	-

2.4. Evaluation of Cream Formulation

2.4.1. Determination of Physical appearance

The prepared cream was studied visually for colour uniformity, homgenity, texture and consistency. Homogeneity and the creamy texture can be examined by rubbing a small quantity of the cream formulation between thumb and index finger. Consistency and presence of coarse particles in the cream can be considered for its homogeneous and smooth nature (Swetha et al, 2023).

2.4.2. Determination of pH

The pH of the formulated cream was determined by standard procedure using pH meter at room temperature. The pH was taken in triplicates (IP, 2014).

2.4.3. Determination of Viscosity

The creams viscosity was determined using Brookfield Viscometer (Model No - DVE51) at different shear rates, with spindle no S-64 at 20rpm at a temperature 25°C as per standard procedure. The values were recorded in triplicates and average calculated (IP, 2014).

2.4.4. Determination of Spreadibility

1gm cream sample was taken between the two glass slides and was compressed for uniform thickness by placing specified gram of weight for about 5 minutes. Then weight was added to the weighing pan. The time in which the upper glass slide moved over the lower side was taken as a measure of spreadability (Swetha et al, 2023).

Spreadibility = W x L/ T

where W=Weight on the upper slide; L=Length moved on the glass slide; T=Time Taken

2.4.5. Dilution Test

The test is to examine the type of cream formulation formed. 1gm of sample when made completely miscible with water and allowed to stand for 10 min. If the cream is o/w type the emulsion is completely miscible with water, while it separates out if it is w/o type of emulsion (Swetha et al, 2023).

2.4.6. Globule size

1gm of cream mixed uniformly with 10ml of glycerin was taken for determination of globule size. A few drops of diluent were mounted on a glass slide and observed under the microscope using eye piece micrometer. A random determination of 200 particle diameter were examined for globule size (Swetha et al, 2023).

2.4.7. Determination of % Release

Skin absorption is an vital route by which substances can enter the body. Absorption through the skin depends on a number of factors, the most important are concentration, duration of contact, solubility of medication, physical condition of the skin and part of the body exposed. The amount of drug absorbed through the skin can be measured directly or indirectly. Static Diffusion Cells is used for release study as per method given by Salamanca et al with minor changes. The egg membrane was used instead of animal skin tissue (Salamanca et al, 2018).

III. RESULTS & DISCUSSION

3.1. Chamomile Extraction: Extraction of flower heads using deionised water was done and the extract solution was used for synthesis of MgO NPs

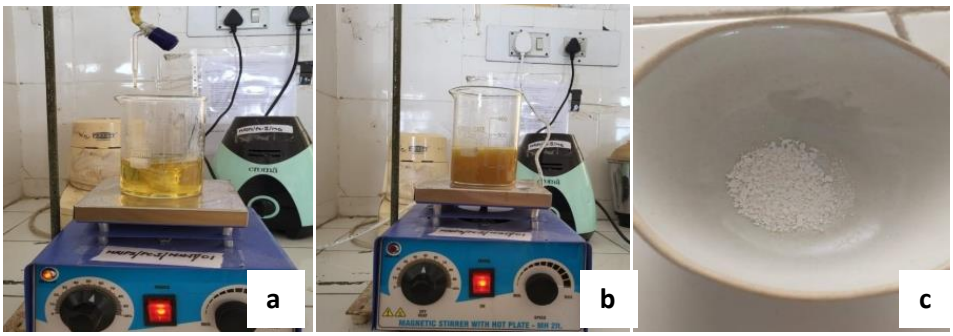

Fig2. Synthesis of MgO NPs a) Addition of Chamomile extract (light yellow) b) Formation of MgO nanoparticles (dark yellow to brown colour) c) Chamomile mediated MgO NPs

3.2. Synthesis of Magnesium oxide Nanoparticles (MgO-NPs)

The nanoparticles were synthesized using aqueous extract of chamomile flowerheads. Formation of nanoparticles was observed with the colour change from light yellow to dark yellowish brown. Further the precipitate was filtered, washed with water and calcinated at 400°C to obtain white amorphous powder. Fig 2 Shows various stages in the synthesis of magnesium oxide nanoparticles

3.3. UV-Vis Spectroscopic analysis & Standard Curve Determination

The UV-Vis spectral analysis of Chamomile extract is shown in Fig 3(a). The spectra shows absorption peak at 266nm. Fig 3(b) and Table No.2 shows the standard curve plot for chamomile extract in aqueous medium.

Table No.2 Determination of Standard Curve of Chamomile extract in water

Concentration (µg/mL)	Absorbance
0.1	0.130
0.2	0.295
0.3	0.434
0.4	0.594
0.5	0.758

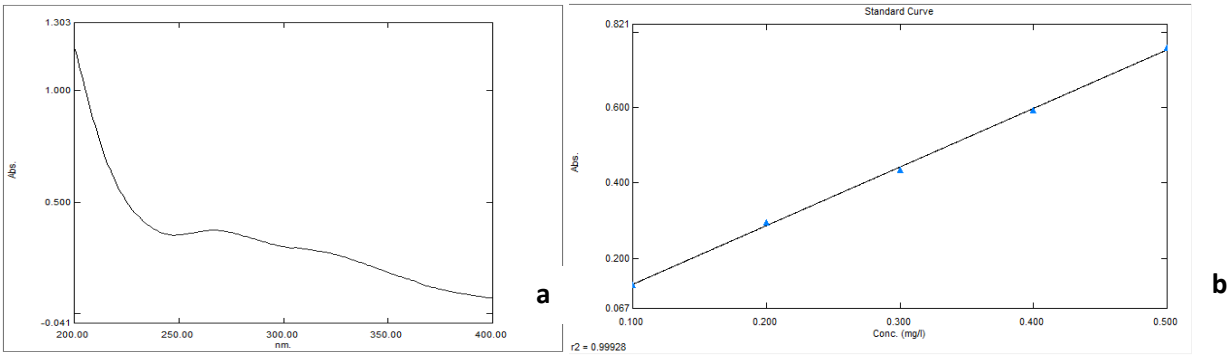

Fig3. a) UV-Vis Spectra of Chamomile Extract
b) Standard Curve of Chamomile extract in water

3.4. FTIR Spectral analysis

The spectral analysis of all the three mentioned above were recorded in Table No: 3 and the FTIR spectra where given in Fig 4 and Fig 5. The study shows not only the chamomile extract is helpful in reducing the metal ions in the process of Nanoparticles synthesis, they are also getting loaded in the nanoparticles which can be advantages in treating many physiological conditions. However, the present study focus on the benefit of Chamomile extract as muscle relaxant that added advantage in the formulation of various muscle relaxant dosage form.

Table No.3 FTIR Spectra of Various Functional groups in Chamomile extract, MgO NPs and MgO NPs in water

Functional Group	Bond	Characteristic IR Frequency range	FTIR of Chamomile-MgO NPs	FTIR of Chamomile Extract	Chamomile-MgO NPs in water
Alcohol	OH stretching	3200-3600 (broad)	3200.42, 3216.78, 3263.38, 3309.98, 3368.88, 3411.98, 3430.82, 3442.50	3353.02	3285.00
Alkene.	C=C Stretching	1620-1680 (weak)	1635.27, 1644.44, 1657.32, 1669.65,	1647.60	1636.91
Alkyne	Terminal ≡C-H Stretching	3250-3350	3263.38, 3309.98		3285.00
Alkane	C-H Stretching	2850-2950	2888.12, 2902.10	2925.88	
Amine	N-H Stretching	3300-3500 (medium)	3368.68, 3411.98, 3430.82, 3442.51, 3491.41	3353.02	

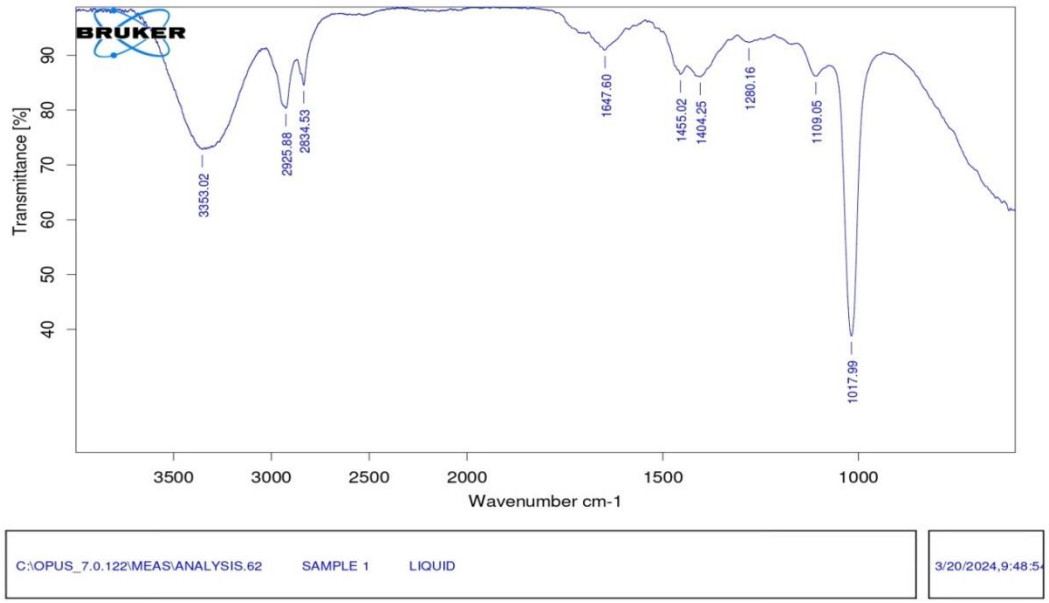

Fig4. FTIR Spectra of Chamomile Extract

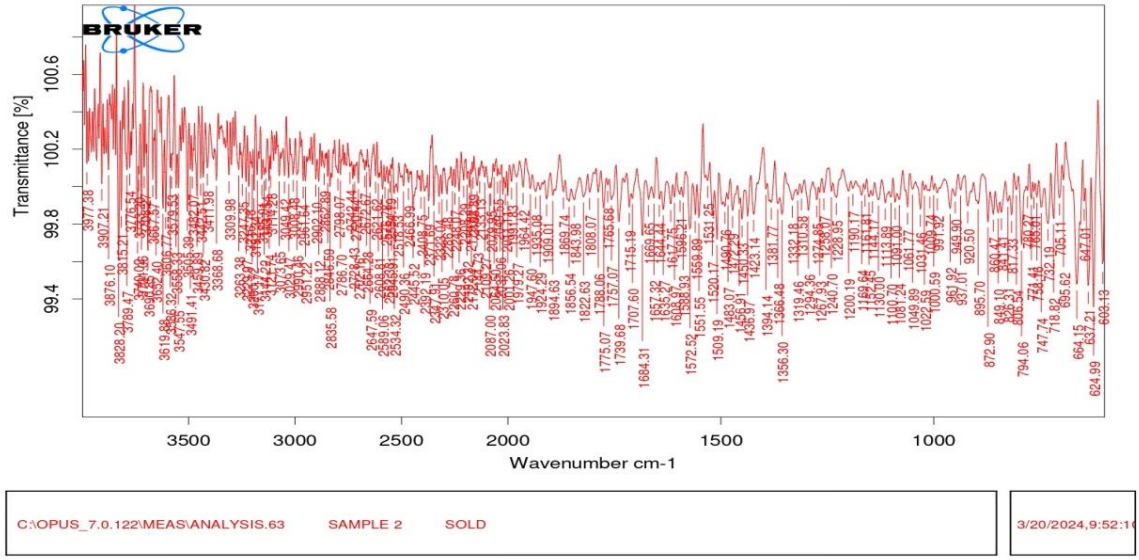

Fig5. FTIR Spectra of Chamomile-MgO NPs

3.5. SEM Analysis

The SEM analysis of MgO NPs can be observed in the Fig 6. The SEM morphology of MgO NPs showed that they have almost spherical to few irregular geometry. With the obtained results the particle size range from 167nm – 195nm.

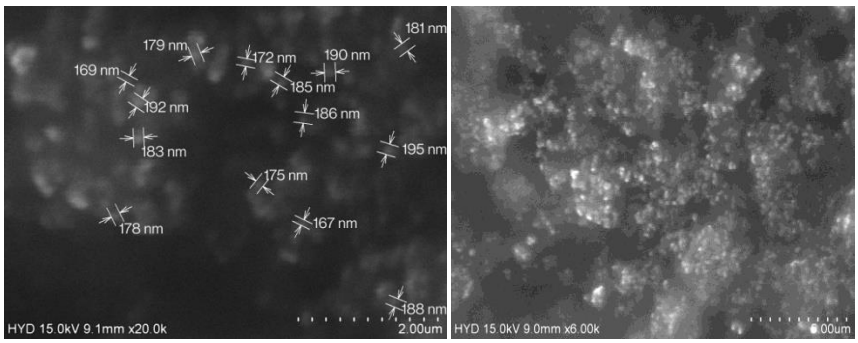

Fig6. SEM structure Analysis of Chamomile-MgO NPs in aqueous medium

3.6. Evaluation of Cream

3.6.1. Physical properties

The cream was observed for its morphological characters showing white colored cream compared with control which is also white in colour. As the colour of CE-MgO NPs itself is white in colour there is no change visibly in the colour of the cream. The cream was also found to be odourless when perfume was not incorporated and has smooth creamy in appearance. The observation is recorded in Table No.4.

3.6.2. Determination of pH

pH of the formulated cream samples and control cold cream was evaluated by digital pH meter. The mean pH of the CE-MgO NPs cream and Control creams are 6.0 and 5.9 respectively. The pH of W/O cream prepared was found all within the normal range of 6–7 while the control cream is slightly acidic. This implies that these creams can be applied on the skin with decreased risk of skin irritation. The human skin has a slightly acidic pH of about 5.5 which allows it to fight infection and other environmental toxins. Use of products that alter the skin pH can affect its protective function. Hence topical products are expected to have a pH range of 6–7 to avoid alteration of the skin pH. The average pH for MgO NPs cream and Control cream is recorded in Table No.4.

Table No.4 Evaluation of MgO nanoparticles cream

Parameter	CE-MgO NPs Cream	Control Cream
Visual Observation	White	White
Spreadability	11.26±0.45	10.4±0.41
pH	6±0.07	5.9±0.04
Dilution Test	Diluted with Oil Phase	Diluted with Oil Phase
Viscosity	4253.3±197.3	4280±144.2
Mean Globule size	48µm to 252µm	36µm to 228µm

3.6.3. Determination of Viscosity

Viscosity is a rheological property of a material which can affect its flow properties. In semi-solid formulations such as creams consist of two immiscible materials, the rheological properties like viscosity and thixotropy .The average viscosity of the formulated cream samples is shown in Table no 4. The cream sample formulated using CE-MgO NPs had similar viscosity compared to control cream samples.

3.6.4. Spreadability Test

The spreadability test evaluates its ability in ease to spread across the skin when applied. the lower the spreadbility value the better its application. The spreadability test for both CE-MgO NPs Cream and Control Cream were performed and the average values were recorded in the Table no.4. The normal range of spreadability of cold cream is between 9.0 to 31.02g.cm/s. The mean spreadability of the creams was found to be 11.26 and 10.4 respectively, which is found to be within limits.

3.6.5. Dilution Test

The solubility of the formulated cream was found to be in liquid paraffin and not water; hence the emulsion is water/oil type of emulsion.

3.6.6. Globule Size

To gain insight on the stability of the formulated sample cream, the globule size and shape were measured and observed using a microscope. Particle size of the formulated cream samples and measurement of the particle size of the cream globules given in Table no.4 and shown in Fig 7.

3.6.7. Determination of % Content Release (Franz Diffusion Cell Method)

The diffusion studies of MgO NPs were studied with Franz Diffusion Cell Method. The experiment were done in triplicate and the results were recorded. Further the cumulative % Drug release were calculated and plotted against time intervals show there is gradual and significant release of CE through 3 hrs of study and it showed an average of 63%. Fig 8 Shows In-vitro % content release.

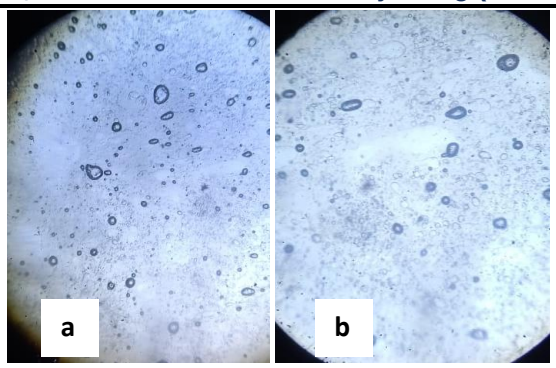

Fig7. Microscopic image of Globule size
a) CE-MgO NPs Cream b) Control Cream

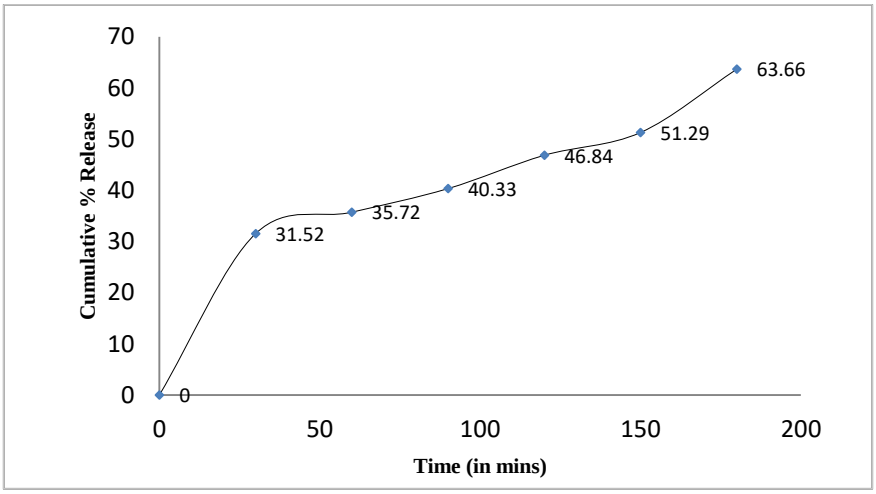

Fig8. In-vitro % Content Release Study of CE-MgO NPs Cream

IV. SUMMARY & CONCLUSION

Nanotechnology has great promise in manipulating things at the atomic level to change many parts of medical treatment, such as diagnosis, monitoring for diseases, operating equipment, regenerative medicine, developing vaccines, and medication delivery. It also opens the way through sophisticated research instruments to develop drugs to improve treatments for various ailments. Nanotechnology can be utilized for medication to particular cells in the body, thereby reducing the risks of failure and rejection. The present study was aimed to prepare nanoparticles through green synthesis using phyto-constituents. Many research works have carried on effective synthesis of NPs using plant extracts. Here, Chamomile extract (CE) was not only used as a catalyst in the production of NPs but it was identified that during the formation of NPs the plant extract is also getting loaded. This was proved with FTIR studies of the MgO NPs and was compared with CE and MgO NPs in water. Initially, aqueous extract of Chamomile flower heads were prepared by normal conventional method. Using co-precipitation method CE initiated MgO NPs were prepared and calcinated. The NPs were characterized by its SEM analysis and FTIR analysis which confirmed loading of CE in the NPs. The nanoparticles were incorporated in to cream formulation as chamomile is a potential stress reliever and also a muscle relaxant. Hence, W/O type cream were prepared and compared with control cream which without NPs. The evaluation test for cream was performed showed all of them are within the limits. Further, the diffusion studies of the cream was performed using Franz diffusion cell method, which shows better release profile during 3hrs period of study. The study can be further refined by simultaneous determination of Mg ions along with CE and research can be extended with various concentrations NPs with different dosage forms which may be therapeutically useful.

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