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# Formulation, Development and Evaluation of Iron Oxide Nanoparticles

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**ABSTRACT:** Cancer is one of the most emerging disease now a days. There is major challenge in front of medical and pharmaceutical science to treat cancer and to avoid different side effects of chemotherapy. Green synthesis of iron oxide nanoparticulate system is best way to tackle with many issues arises due to chemotherapy. In the green synthesis technique nanoparticles are prepared by using herbal extract hence they may less toxic and show less side effects as compared to chemotherapeutic treatment. Some herbal extract itself acts as reducing agent hence there is no requirement of other synthetic reducing agent or stabilizing agent. Nanoparticulate drug delivery system is most prominent and effective than other drug delivery system. In the nanoparticulate drug delivery system magnetic nanoparticles will be better option as magnetic targeting drug delivery system there are many magnetic metals are available but in that iron is economical metal beside that iron oxide nanoparticles shows potential applications in biomedical field it also shows different properties that's why it used in many biomedical applications such as biocompatibility, supermagnetism, high saturation magnetization and low toxicity. Other than these properties they are only type of nanoparticles that are approved by food and drug administration for clinical use. The approach of this research is to make simple rapid and non-toxic synthesis of nanoparticles and which can be useful in treatment of cancer without major side effects and green synthesis helps to avoid some drawbacks which arises due to synthetic method of nanoparticles preparation.

**KEYWORDS:** Cancer, chemotherapy, magnetic nanoparticles, hyperthermia, magnetic targeting.

## I. INTRODUCTION:

Cancer is the most emerging disease now a days. One in three people develop cancer during their life time. There were so many therapies are evolved to treat cancer it include chemotherapy

which is expensive treatment and it will show many side effects because they toxic to all cells including cancerous and normal cells also. Sometimes cell resistance may developed with drug used in cancer chemotherapy i.e multi drug resistance.

All the problems or difficulties in the treatment of cancer can be defeated by nanoparticulate drug delivery system. In the branch of nanoparticulate drug delivery magnetic nanoparticles will give best result in treatment of cancer as magnetic targeting drug delivery system. Iron oxide nanoparticles are economical than any other magnetic metal.

During last decades, iron oxide nanoparticles show potential applications in biomedical field as well as pharmaceutical field. Beside of these it also frequently encountered in most applications because of their biocompatibility, supermagnetism, high saturation magnetization and low toxicity. They are also the only type of nanoparticles that are approved by food and drug administration for clinical use.

There are many methods are available for synthesis of iron oxide nanoparticles with the aim to produce nanoparticles of different sizes, shapes, and use for biomedical purpose but all are synthetic methods they have some drawbacks such as low production rate, high energy consumption and high cost, the usage of reducing agent or stabilizers may cause many toxic effect and it may hazardous to environment thus, there is essential to develop eco-friendly nanoparticles in which there is no use of hazardous chemicals in their synthesis.

In this research we explore the green synthesis of iron oxide nanoparticles by using leaf extract of camellia sinensis (green tea). Leaves extract of green tea consist of flavonoids and

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polyphenols. They act as reducing and stabilizing agent.

The synthesis of iron oxide nanoparticles by reduction of aqueous $Fe^{3+}$ and $Fe^{2+}$ ions with leaf extract of green tea main reaction is reduction for synthesis of nanoparticles.

Metallic nanoparticles have proved their novel application in medical field to diagnose and treat various types of cancer in addition to that both herbal plants possess the anticancer activity as they contains flavonoids and polyphenols.

The main aim of this research is to produce biobased nanoparticles are new revolutionized to treat malignant deposite without interfering normal cells.

Herbal medicines have been widely used all over the world since ancient times and they have better therapeutic value and fewer adverse effects as compared to synthetic drug. [1-3]

## II. MATERIALS AND METHODS:

Plant selected for this experimental work is Camellia sinensis i.e green tea leaves (Lipton green tea), as this consist of catechin, polyphenols and flavonoids as active chemical constituents which are also act as reducing agent and capping agent and support to the synthesis of nanoparticles. The metal precursor used is ferric chloride purchased from NM pharma[4].

## III. PREPRATION OF GREEN TEA LEAVES EXTRACT:

Green tea extract is prepared by maceration process which can be prepared as follows:

Weigh about 5gm of green tea powder.Add this to 200 ml of deionized water, stirr it properly.Then keep it on water bath at $80^0$C for 60 min. Filter it by using whatman filter paper no. 4 Store it in refrigerator for further use.[5]

## IV. SYNTHESIS OF NANOPARTICLES:

Add 0.1M Ferric chloride and green tea extract with 1:1 ratio Stirr it properly while mixing Adjust pH upto 7 using pH meter by dropwise addition of 0.1 M NaOH Centrifuge the final solution with the help of micro centrifuge machine up to 7000rpm to remove impurity. Wash with distilled water to remove impurity if any. Then discard supernant and separate nanoparticles in petri plate and dry it on the hot plate at $60^0$C.

## V. EXPERIMENTAL DESIGN OF NANOPARTICLES:

In the present work trial batches of nanoparticles were optimized using $3^2$ factorial design using the design expert software( design expert version 11) the parameter such as iron salt and extract ratio and rotation per minute are independent variable to study different levels i.e. ratio of iron salt and extract 0.5:1(-1 level), 1:1(0 level) and 1:1.5(+1 level). rpm 5000(-1 level), 6000(0 level) and 7000(+1 level). Particle size and zeta potential were dependent variable.[6-8]

| Batch No. | Extract (ml) | Iron salt (ml) | Rpm | NaOH (ml) |
|---|---|---|---|---|
| $F_1$ | 1 | 0.5 | 5000 | 5 |
| $F_2$ | 1 | 0.5 | 7000 | 5 |
| $F_3$ | 1 | 1 | 4318.21 | 5 |
| $F_4$ | 1 | 0.5 | 7000 | 5 |
| $F_5$ | 1 | 1.5 | 5000 | 5 |
| $F_6$ | 1 | 1 | 6000 | 5 |
| $F_7$ | 1 | 1.5 | 5000 | 5 |
| $F_8$ | 1 | 1.5 | 7000 | 5 |
| $F_9$ | 1 | 1.8 | 6000 | 5 |

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Thus total 9 batches of nanoparticles were prepared and stored at $25^0$C and used for further evaluation study:

| Sr. No. | Name of batches | Particle size (nm) | Zeta potential (mv) |
|---|---|---|---|
| 1. | $F_1$ | 69.4 | 4.3 |
| 2. | $F_2$ | 1305.1 | -0.7 |
| 3. | $F_3$ | 119 | -0.7 |
| 4. | $F_4$ | 165 | 0.9 |
| 5. | $F_5$ | 419 | -0.0 |
| 6. | $F_6$ | 88.7 | -32.5 |
| 7. | $F_7$ | 347 | 0.4 |
| 8. | $F_8$ | 6373.4 | -2.2 |
| 9. | $F_9$ | 374.8 | -2.3 |

From above observation it was found that batch $F_6$ shows the results which are in the range for both particle size and zeta potential i.e. 88.7nm and -32.5mv respectively.

## VI. RESULT:

**1. Appearance of nanoparticles:**

**2. % Practical yield:**

Quantity of extract used: 0.35 gm

Quantity of nanoparticles formed: 0.28 gm

$$\% \text{ Practical yield} = \frac{\text{Quantity of nanoparticle formed} \times 100}{\text{Quantity of extract used}}$$

$$= \frac{0.28 \times 100}{0.35}$$

$$= 80\%$$

3. FTIR:

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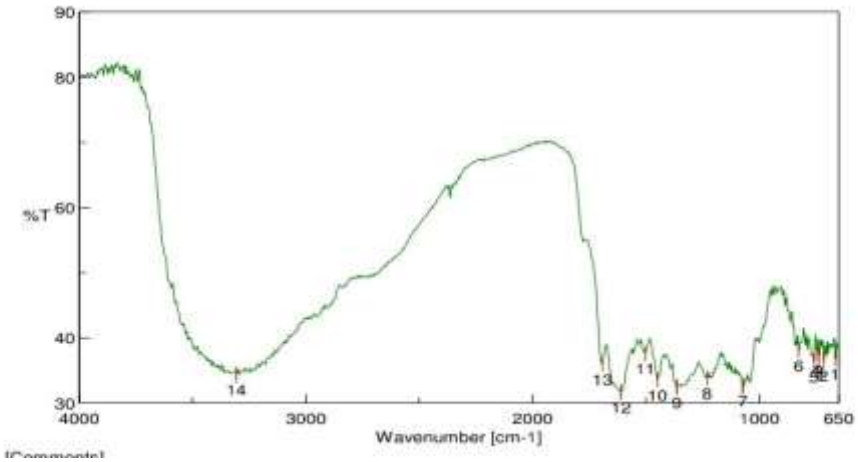


| Sr. no. | Observed ($cm^{-1}$) IR Frequency | Group identified |
|---|---|---|
| 1. | 3307 | O-H Stretching |
| 2. | 1693 | C-H Stretching |
| 3. | 1610 | C=C Stretching |
| 4. | 1364 | C-N Stretching |
| 5. | 1074 | C-O-C Stretching |

**4. Particle size:**

ANOVA

The model F- value of 3.41 implise the model is significant. There is only a 3.02% chance that an F- value this large could occur due to noise.

P –value less than 0.0500 indicate model terms are significant. In this case there are no significant model terms. Value greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy ), model reduction may improve your model.

| Source | Sum of squares | df | Mean squares | F- Value | P-Value | |
|---|---|---|---|---|---|---|
| Model | 2.358E+07 | 6 | 3.930E+06 | 3.41 | 0.0302 | Significant |
| A- Ratio | 2.077E+06 | 1 | 2.077E+06 | 1.80 | 0.2025 | |
| B- Ratio | 2.602E+06 | 1 | 2.602E+06 | 2.26 | 0.1568 | |
| AB | 5.368E+06 | 1 | 5.386E+06 | 4.66 | 0.0502 | |
| Residual | 1.498E+07 | 10 | 1.153E+06 | | | |
| Cor total | 3.856E+07 | 16 | | | | |

Interaction report: Particle size

The interaction report showed that as we increases the ratio of extract: FeCl3 then particle size also increases and if decreases the ratio the particle size also decreases, thus we chose the ratio 1:1 then we get paticle size less than 100.

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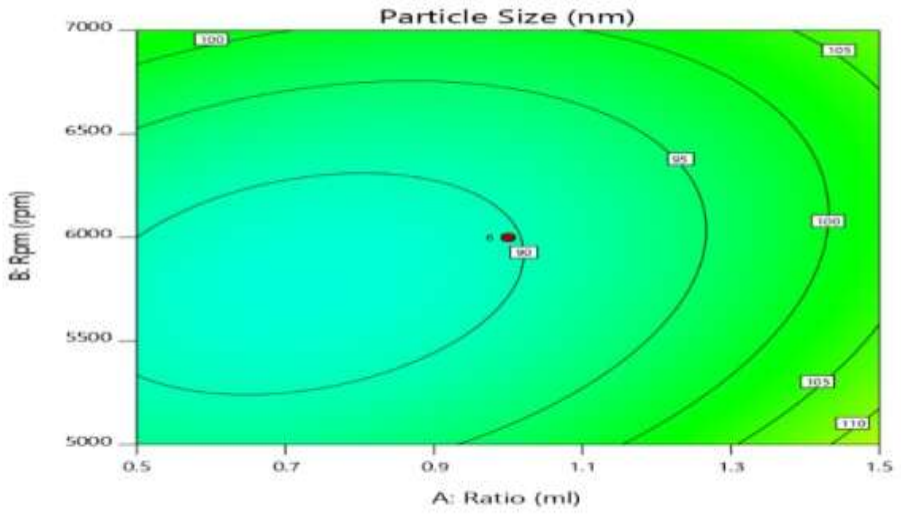
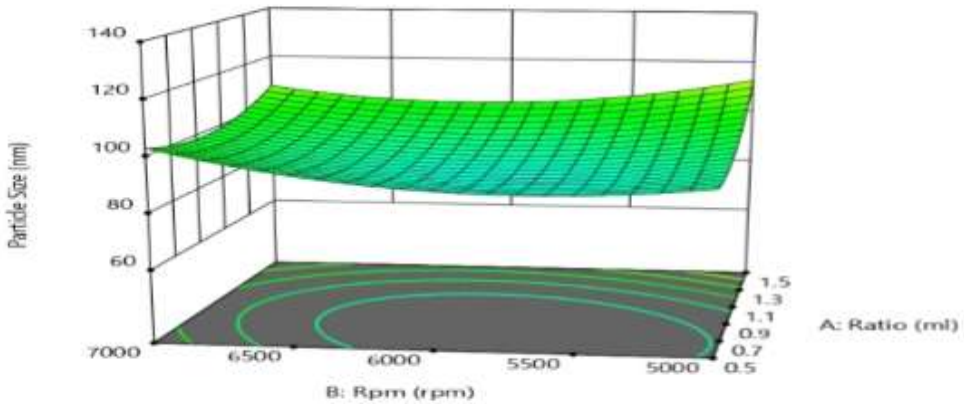



**Two dimensional contour plot for particle size**

3D plot for particle size:

The three dimensional plots showed that conc. Of FeCl3 increases it also increase particle size, the optimum particle size is observed in formulation with particle size 87.5nm which has ratio conc. of extract and salt is 1:1, while the rpm of centrifuge is 6000 rpm as particle size also increases with increase in rpm.




**Three Dimensional Response surface plot for particle size**

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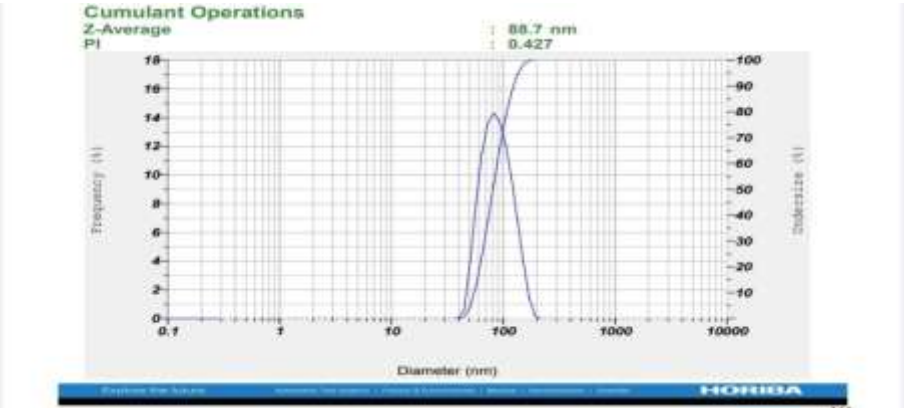



**Particle size of optimized batch**

**5. Zeta potential:**

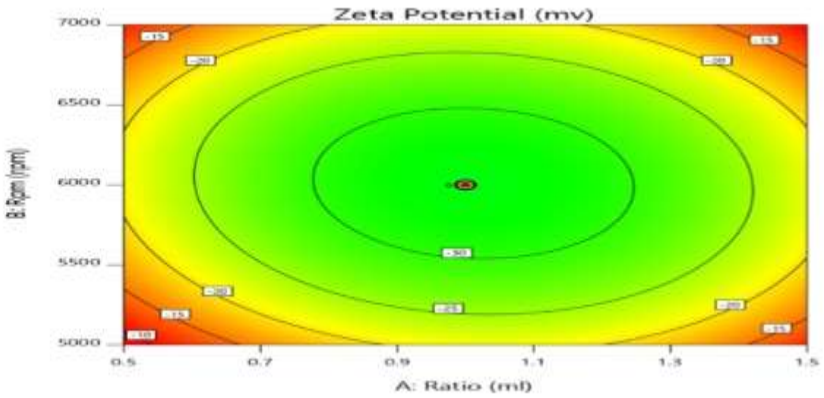
ANOVA:

The model F-value of 263.60 implise the model is significant. There is only a 0.01% chance that an F- value this large could occur due to noise. P- values less than 0.0500 indicate model term significant. values greater than 0.1000 indicate the model term are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

| Source | Sum of squares | df | Mean squares | F- Value | P-Value | |
|---|---|---|---|---|---|---|
| Model | 4509.00 | 3 | 501.00 | 263.60 | 0.0001 | Significant |
| A- Ratio | 4.01 | 1 | 4.01 | 2.11 | 0.1770 | |
| B- Ratio | 0.8374 | 1 | 0.8374 | 0.4406 | 0.5218 | |
| AB | 13.52 | 1 | 13.52 | 7.11 | 0.0236 | |
| Residual | 19 | 4 | 1.90 | | | |
| Cor total | 4528.01 | 7 | | | | |

Interaction report: zeta potential

Zeta potential also increases with increase in the conc. of iron salt and rpm of centrifuge also affect the zeta potential As it icreases zeta potential also increases.




**Two dimensional contour plot for zeta potential**

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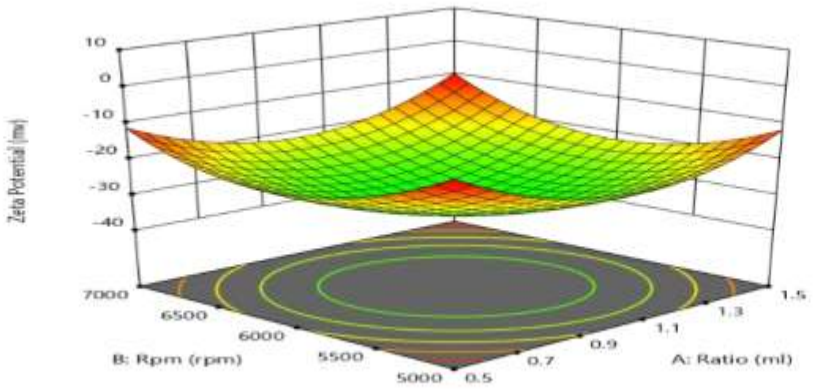
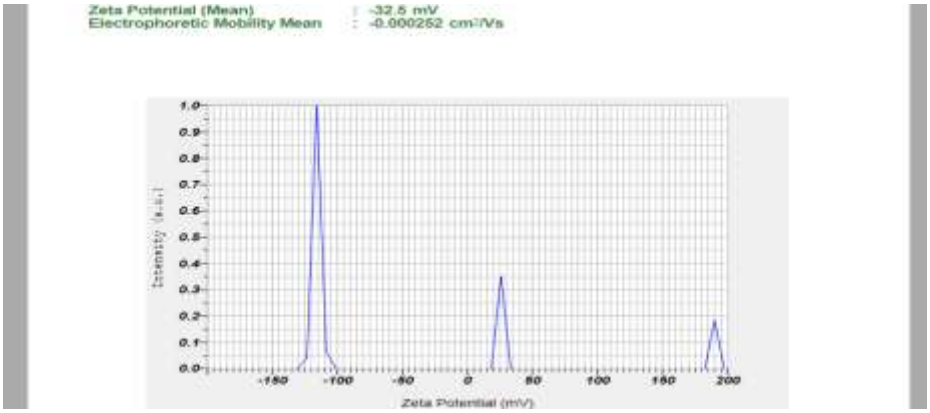
3D plot for zeta potential:

The three dimensional plots showed that conc. of FeCl3 increases zeta potential also increases, the optimum zeta potential is observed in formulation with particle size -32.5mv which has ratio conc. of extract and salt is 1:1, while the rpm of centrifuge is 6000 rpm as zeta potential also increases with increase in rpm.




**Three dimensional response surface plot for zeta potential**




**Zeta potential of optimized batch**

## VII. DISCUSSION:

Cancer is one of the most emerging disease now a days. There is major challenge infront of medical and pharmaceutical science to treat cancer and to avoid different side effects of chemotherapy. Green synthesis of iron oxide nanoparticulate system is best way to tackle with many issues arises due to chemotherapy. In the green synthesis technique nanoparticles are prepared by using green tea extract hence they may less toxic and show less side effects as compared to chemotherapeutic treatment. Green tea extract having property that it act as reducing agent also hence there is no requirement of other synthetic reducing agent or stabilizing agent. Nanoparticulate drug delivery system is most prominent and effective than other drug delivery system and it deals with new technologies for developing personalized drug delivery system. Magnetic nanoparticles will be better option as magnetic targeting drug delivery system, there are many magnetic metals are available but iron is economical metal beside that iron oxide nanoparticles shows potential application in biomedical field, it alo approved by FDA. Iron oxide nanoparticles are biocompatible, supermagnetism, high saturation magnetization and low toxicity.

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## VIII. CONCLUSION:

In this present work iron oxide nanoparticles were synthesized sucessfully in an easy and less time consuming way using camellia sinensis leaves extract. The polyphenols in the green tea extract may possess the property of reducing the ferric cation and also act as capping agent. These nanoparticles reduces the use of harmful chemicals as compared to nanoparticles formed by synthetic methods.

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