Sahand university of technology

Synthesis and investigation of plasma modified mesoporous silica nanostructured properties obtained from cereals husk and their application in drug delivery

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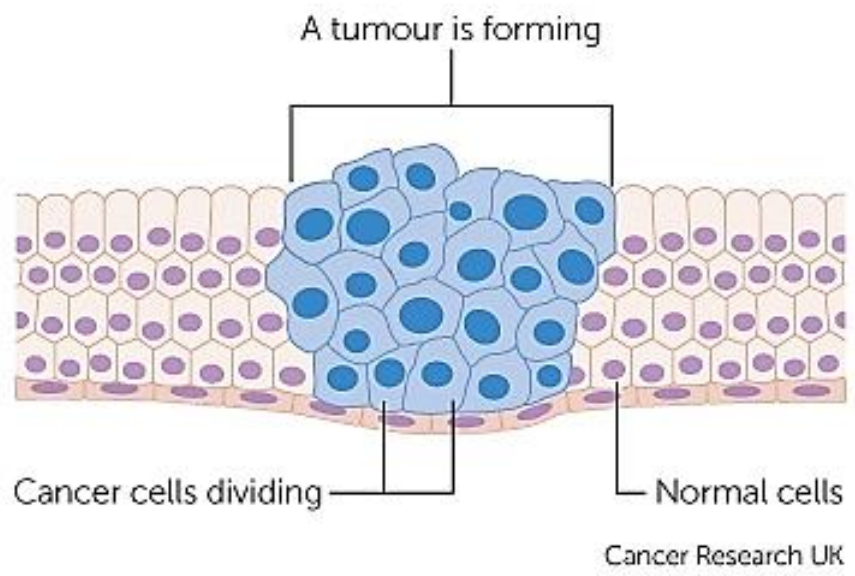
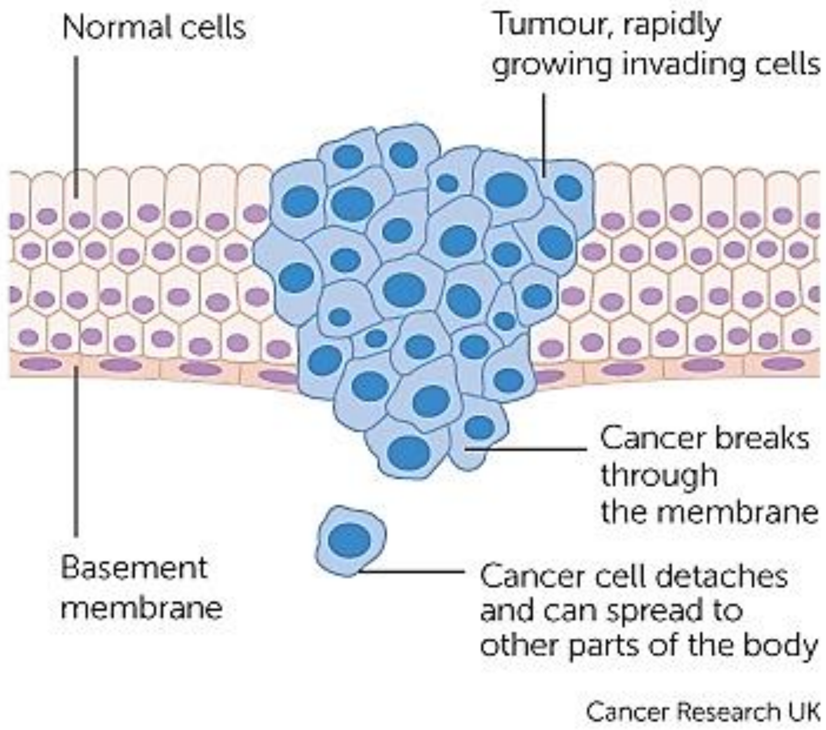
Outline

- Introduction
- Literature Review
- Motivations
- Research Gap
- Thesis Objectives
- Research Methodology
- Time Table

Introduction

➢ Cancer is when abnormal cells divide in an uncontrolled way. Some cancers may eventually spread into other tissues

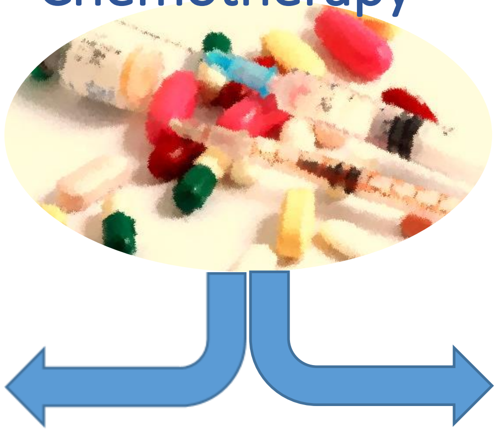




Introduction

- Chemotherapy has side effects to body
- Chemotherapy drugs can destroyed by enzymes
- Tis method is not private

Chemotherapy

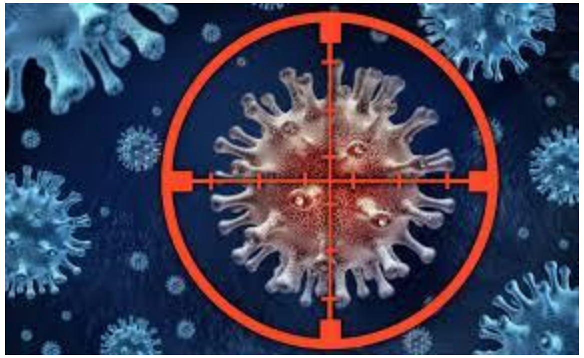


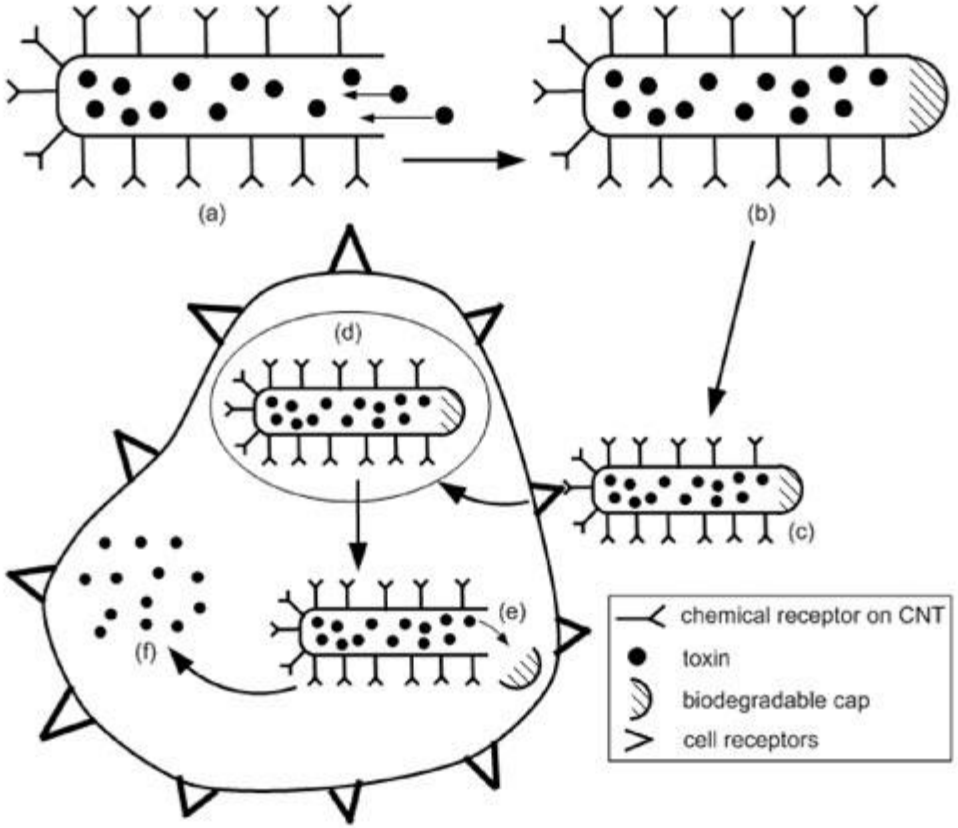
Introduction

- What's the solution?

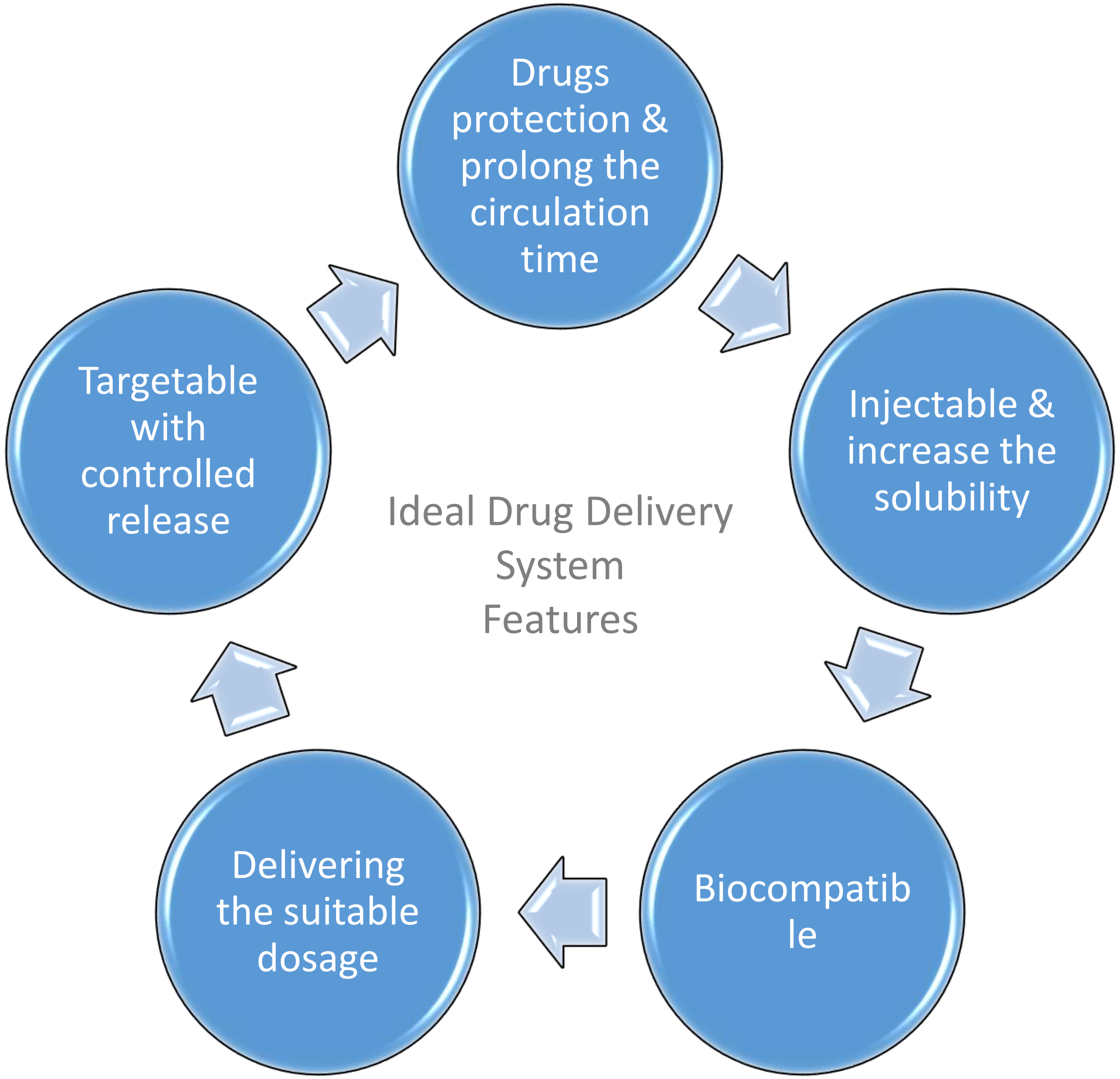
Paul Ehrlich
1991

Magic bullet, or shot in the dark?





Introduction



Introduction

Drug Delivery system (DDS)

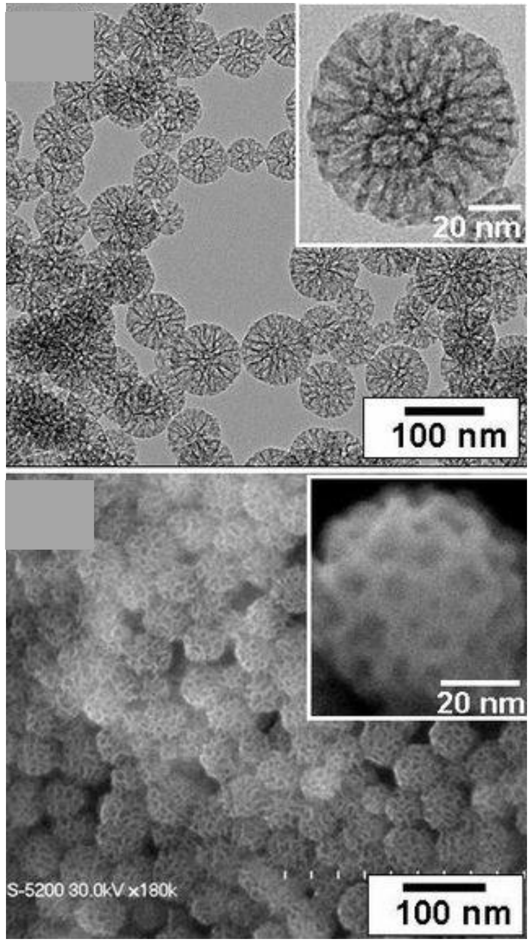
Nanocarrier
- ✓ High surface area
- ✓ High pore volume
- ✓ Stable structure
- ✓ Controllable morphology
- ✓ Ability to modification &…

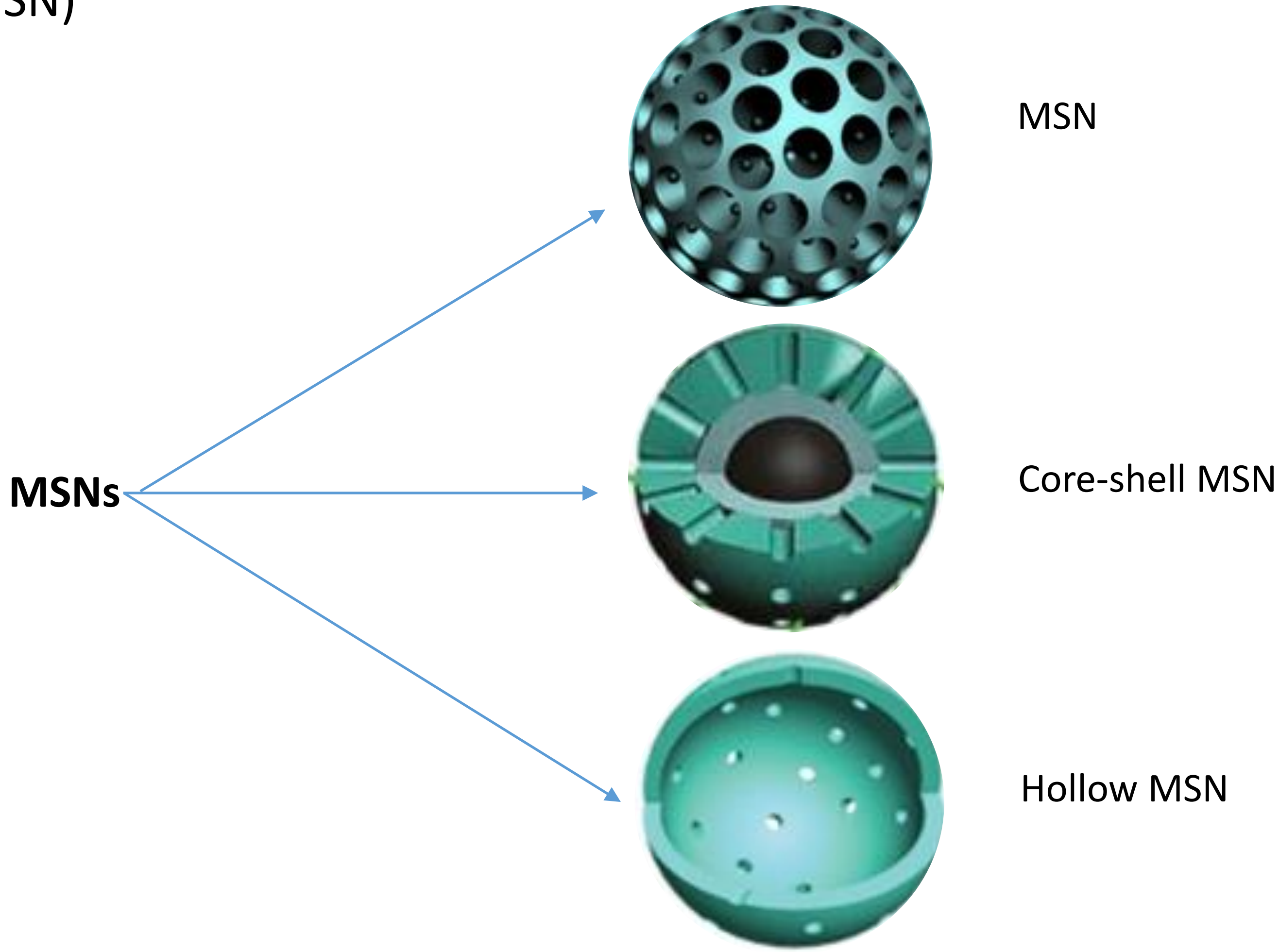
Targeting agent
- ✓ Active
  - ✓ Monoclonal antibodies
  - ✓ Aptamer targeting molecules
  - ✓ Oligopeptide-based targeting molecules
  - ✓ Folate-based targeting molecules
- ✓ Passive
  - ✓ Tumor abnormal blood vessels (EPR effect)
  - ✓ Tumor microenvironment features
    - Enzymes
    - pH
    - Temperature

Controlled release by stimuli-responsive systems
- ✓ Internal
  - Enzymes
  - pH
  - Temperature
  - Redox
- ✓ External
  - Magnetic field
  - Ultra sound
  - Light

Introduction

➢ Mesoporous Silica Nanoparticle (MSN)





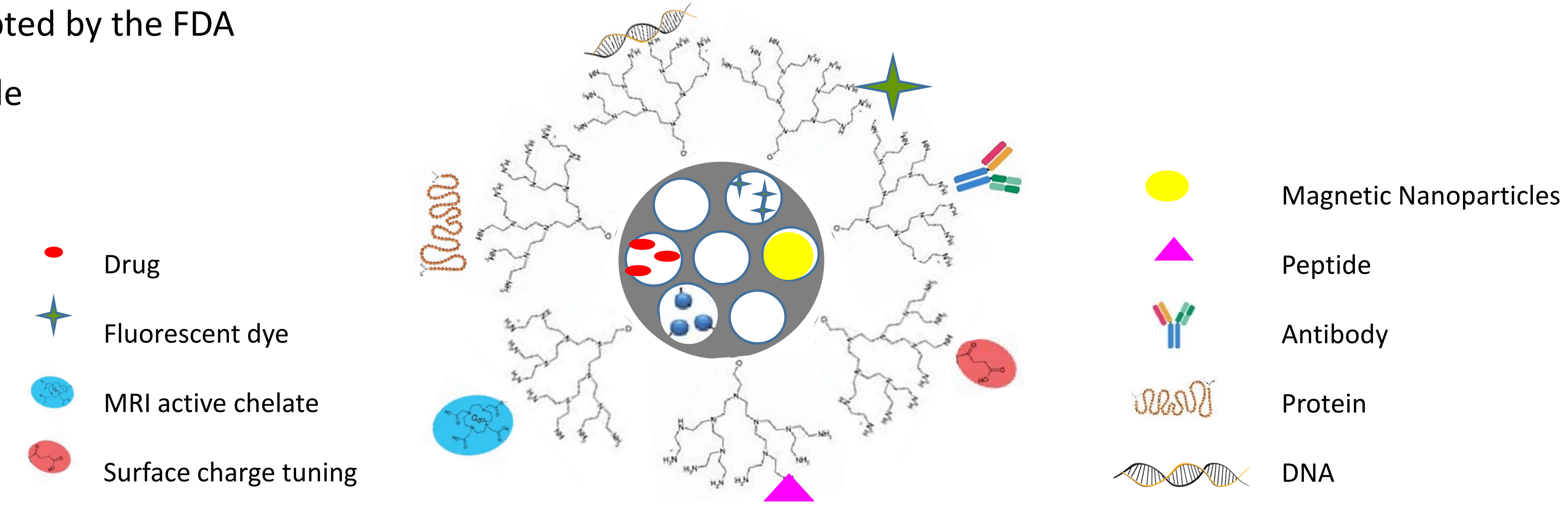
Introduction

Features

- Stable structure
- Uniform particle size
- Large surface area
- High pore volume
- Tunable pore diameters
- Covered by silanol groups
- MSN is accepted by the FDA
- Biocompatible

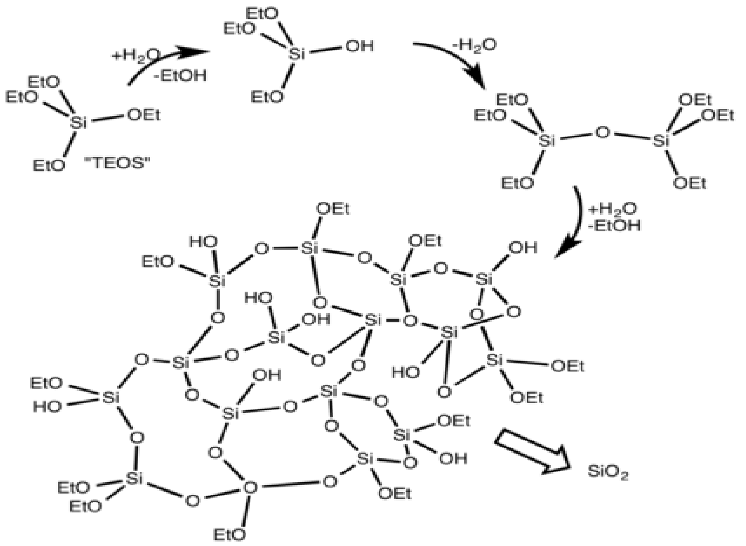
⟹

- Ability to encapsulate a variety of therapeutic agents such as drugs, fluorescent dyes & MRI active chelate
- High drug loading capacity
- surface modifications with functional groups
- Controlled release with stimuli-responsive systems
- Sustained release

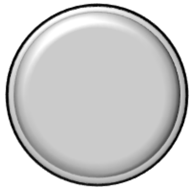


Introduction

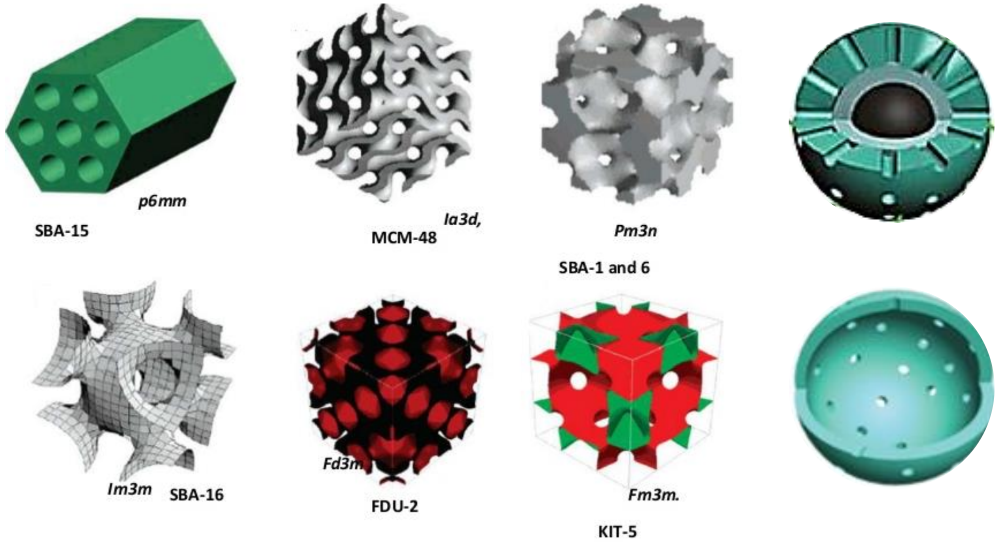
Mesoporous Silica Nanoparticles synthesis



- Stöber method → Silica nanoparticles
- Modified stöber method → Mesoporous silica nanoparticles



Templates as
structure directing agent



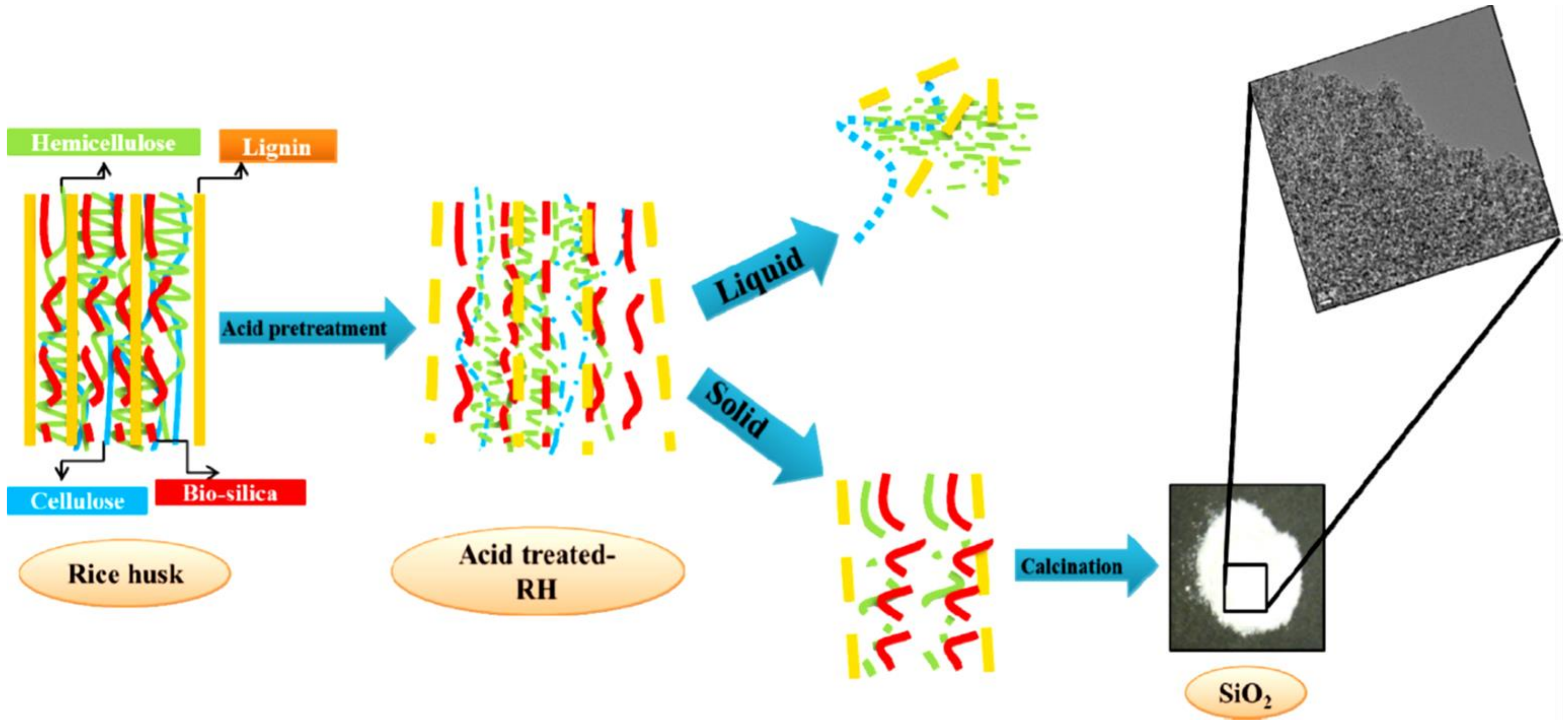
Introduction

- Precursors
  - Metal alkoxide
    - TEOS
    - TMOS
    - MTES
    - MPS
  - Inorganic metal salts → Na2SiO3 that can extracted from cereal husks

- Lignocellulose: 72-85 %
- Silica: 15-28 %

Introduction

- Silica Nanoparticles synthesis from cereal husks

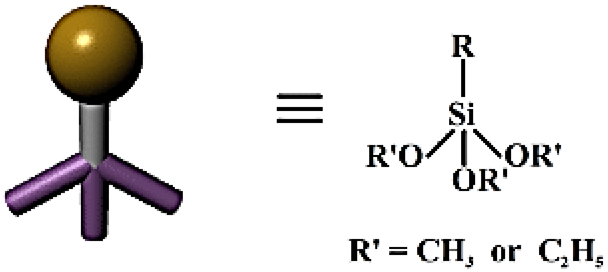


- $SiO_2 + NaOH \rightarrow Na_2SiO_3 + H_2O$

Introduction

➢ Mesoporous Silica Nanoparticles modification

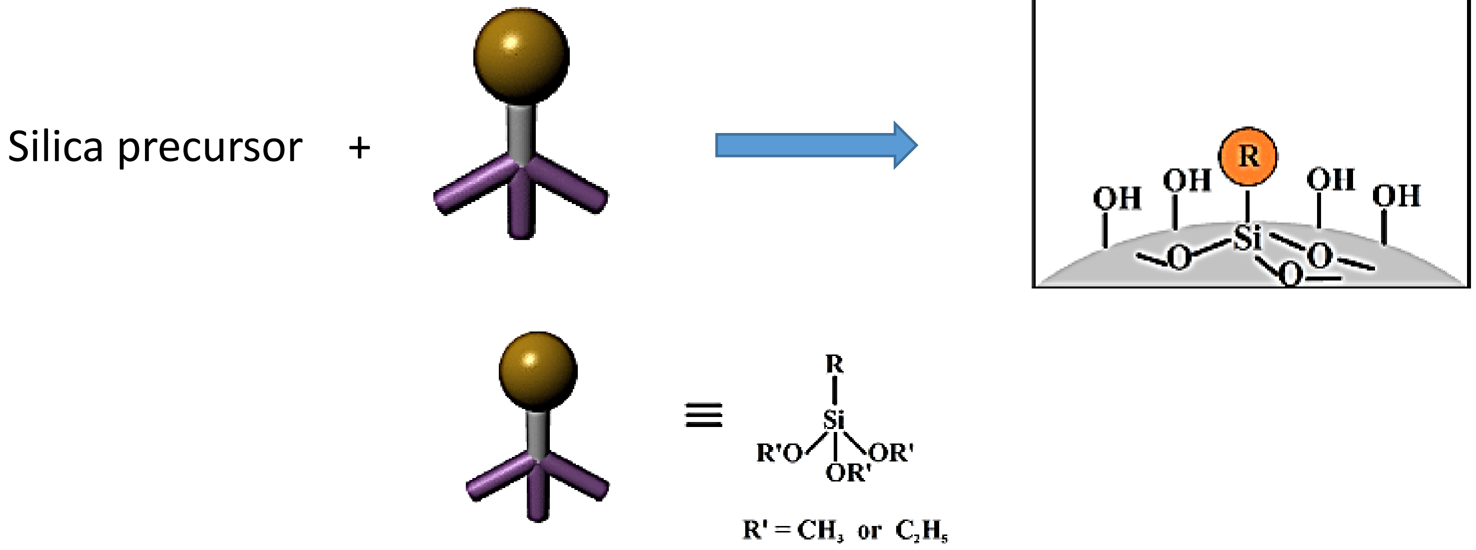
→ Post synthesis grafting



Alkoxysilane

Introduction

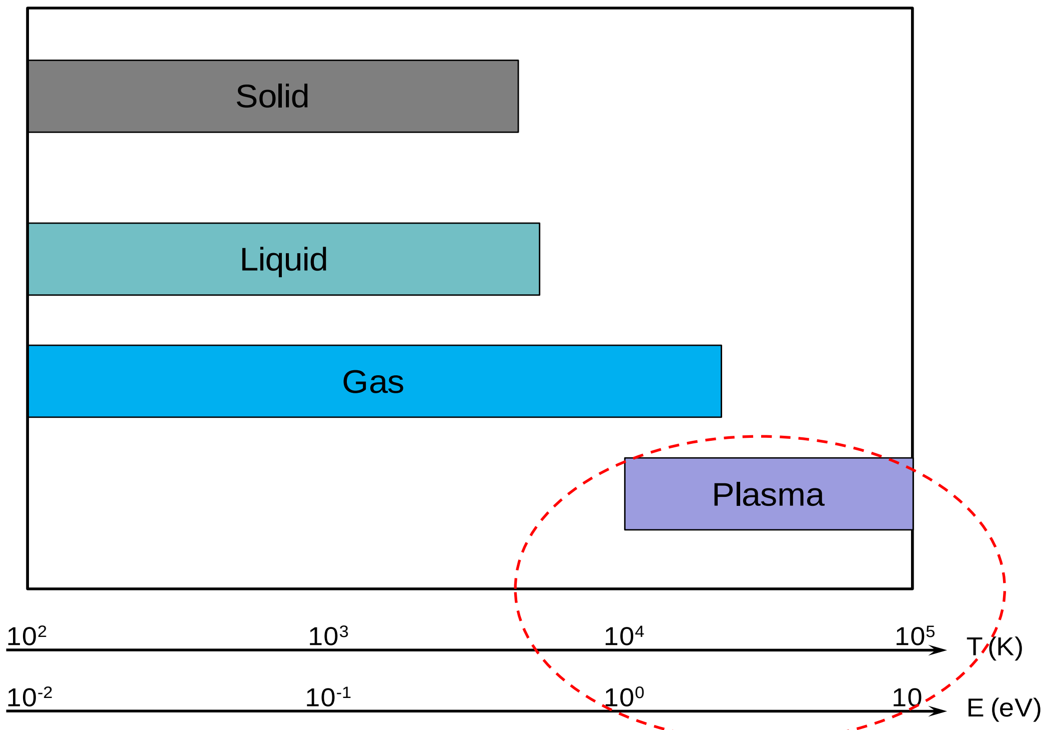
- Mesoporous Silica Nanoparticles modification
  - Post synthesis grafting
  - Co-condensation



Introduction

Plasma

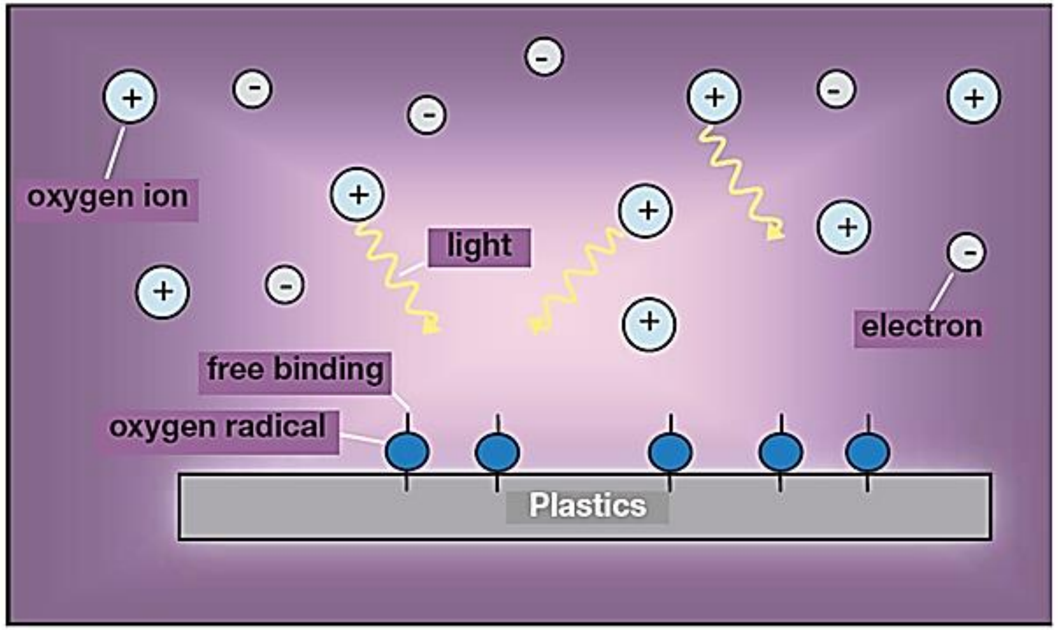
- Plasma can be defined as a quasi-neutral gas of charged and neutral particles characterized by a collective behavior



Introduction

Species in Plasma

- Electrons
- Positive ions
- Negative ions
- Electronically excited atoms and molecules
- Vibrationally and Rotationally excited molecules
- Active Radicals
- UV ultraviolet light photons
- Neutral species



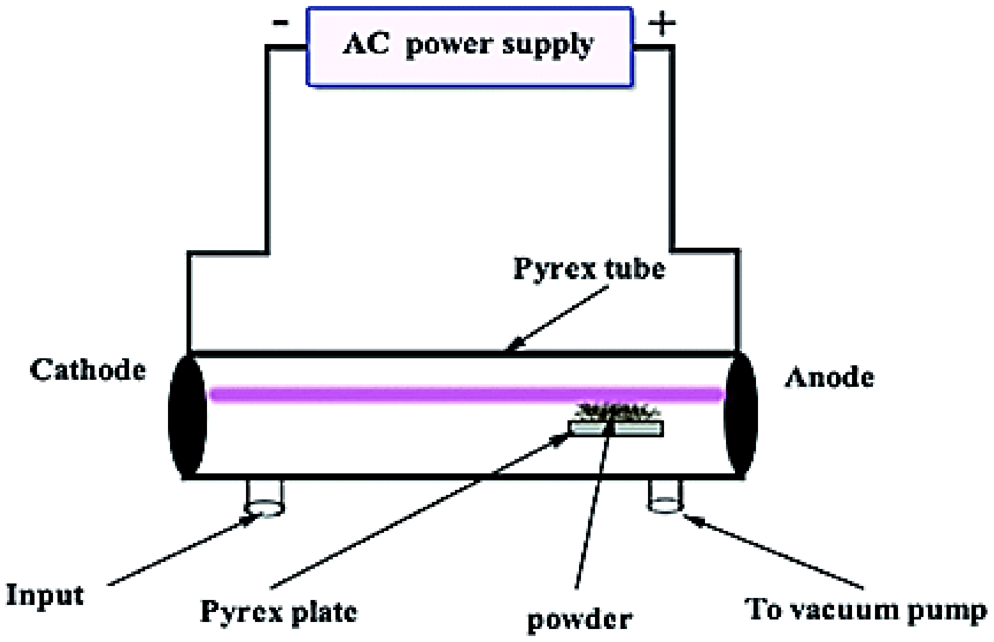
Introduction

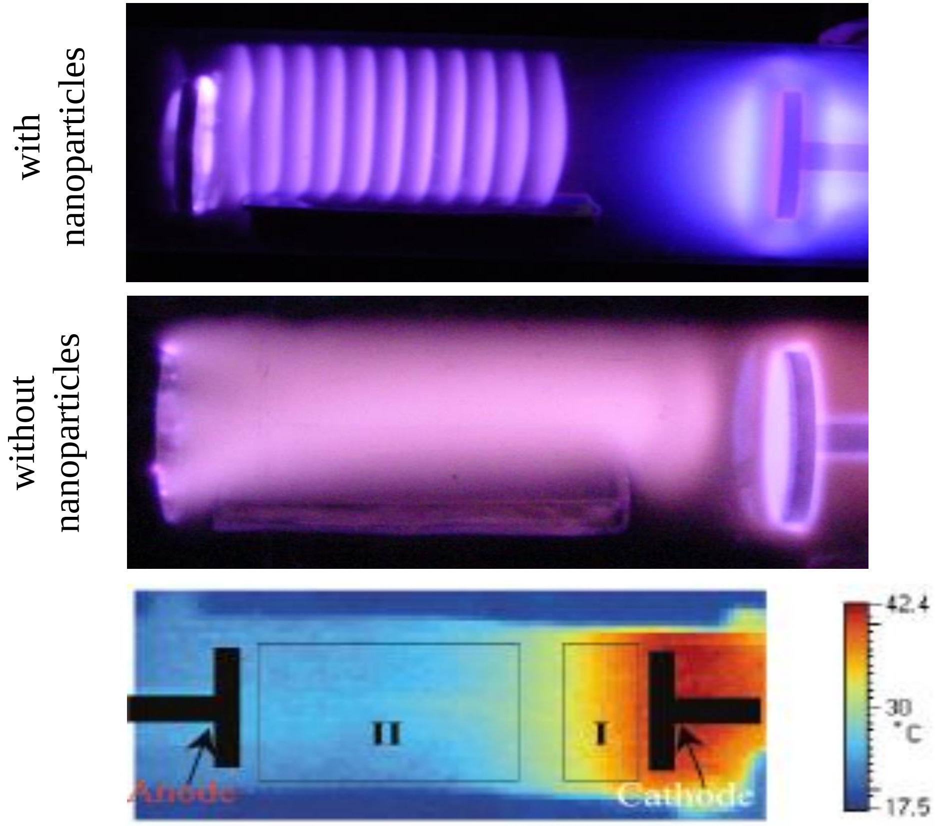
➢ Depending on their energy level, temperature and pressure, plasmas are usually classified as:

	Thermal Plasma	Cold Plasma
Temperature	• High electron temperature • High gas temperature	• High electron temperature • Low gas temperature
Pressure	Atmospheric or higher	Low ($<$ 0.1 bar) for most cases
Appearance	Filamentary inhomogeneous	Homogeneous
Types	• Plasma jet • DC corona torch • arc	• Glow • Radio Frequency • Microwave
Uses	• Ultra-fine particles spraying • Sputtering	Modification or treatment of particles surface

Introduction

Glow discharge plasma

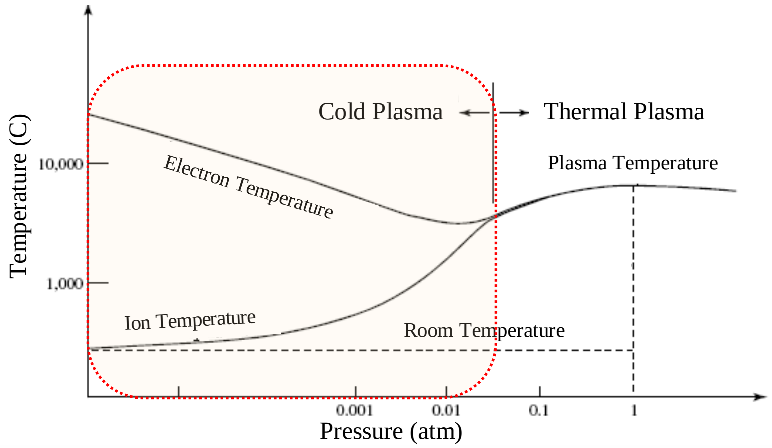


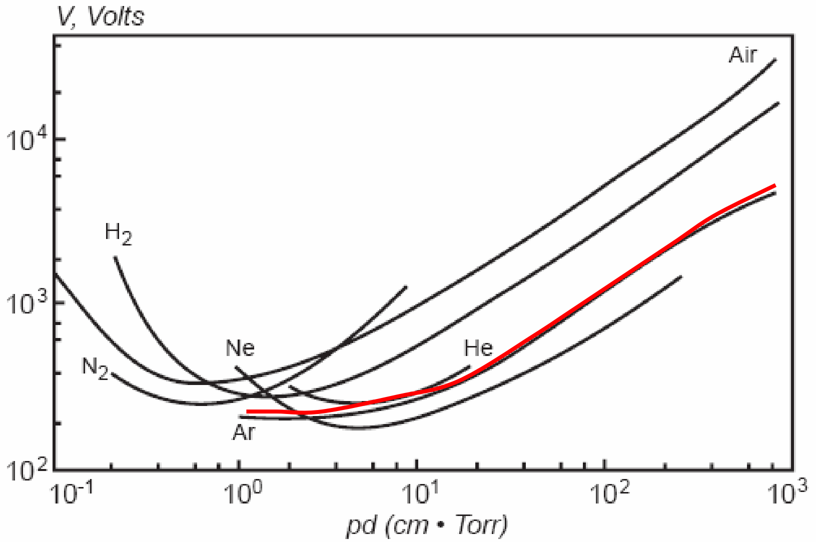


Introduction

Glow discharge plasma

- Voltage: 1000 – 5000 V
- Current: 100 mA
- Bulk Temp: Room Temperature
- Electron Temp:10000 C
- Ion Temp:1000 C
- Pressure:0.1-10 torr
- Distance of Electrodes for Ar: 10 – 30 cm





Literature review

Mesoporous silica Nanoparticles

- Silica nanoparticles from rice husk
- Modification by plasma
- Silica nanoparticles in drug delivery

Literature review

➢ **Silica nanoparticles from rice husk**

In 1938 existence of silica in RH was Discovered

-Synthesis amorphous and crystalline silica from direct calcination of RH.

Water pretreatment

-Water leaching of raw RH to remove adhering soil, dust, and some metal cations.

-Water rinse can effectively remove most minerals except for K and Ca in RH.

Acid pretreatment

-To completely remove metal impurities and carbonaceous residue.

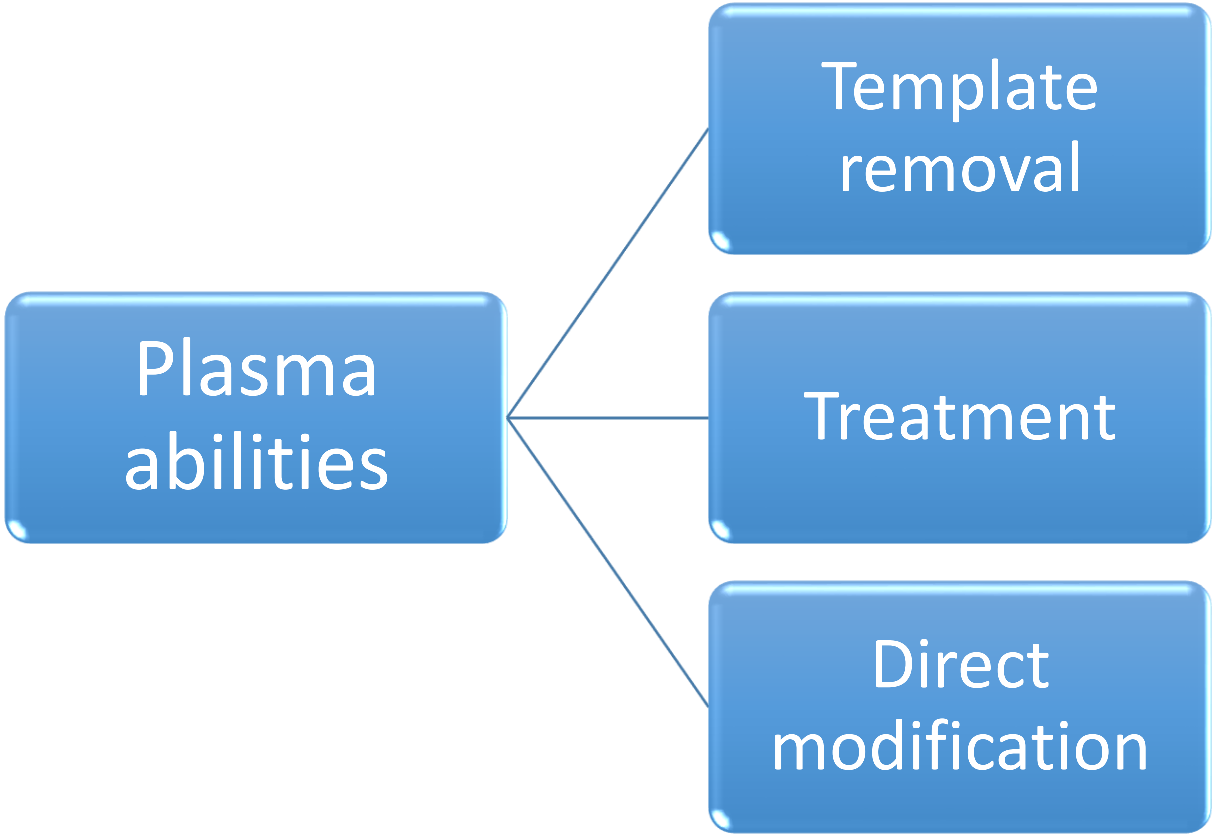
- HCl

-H_2SO_4

-Organic acids, such as acetic acid, oxalic acid, citric acid and carboxylic acid

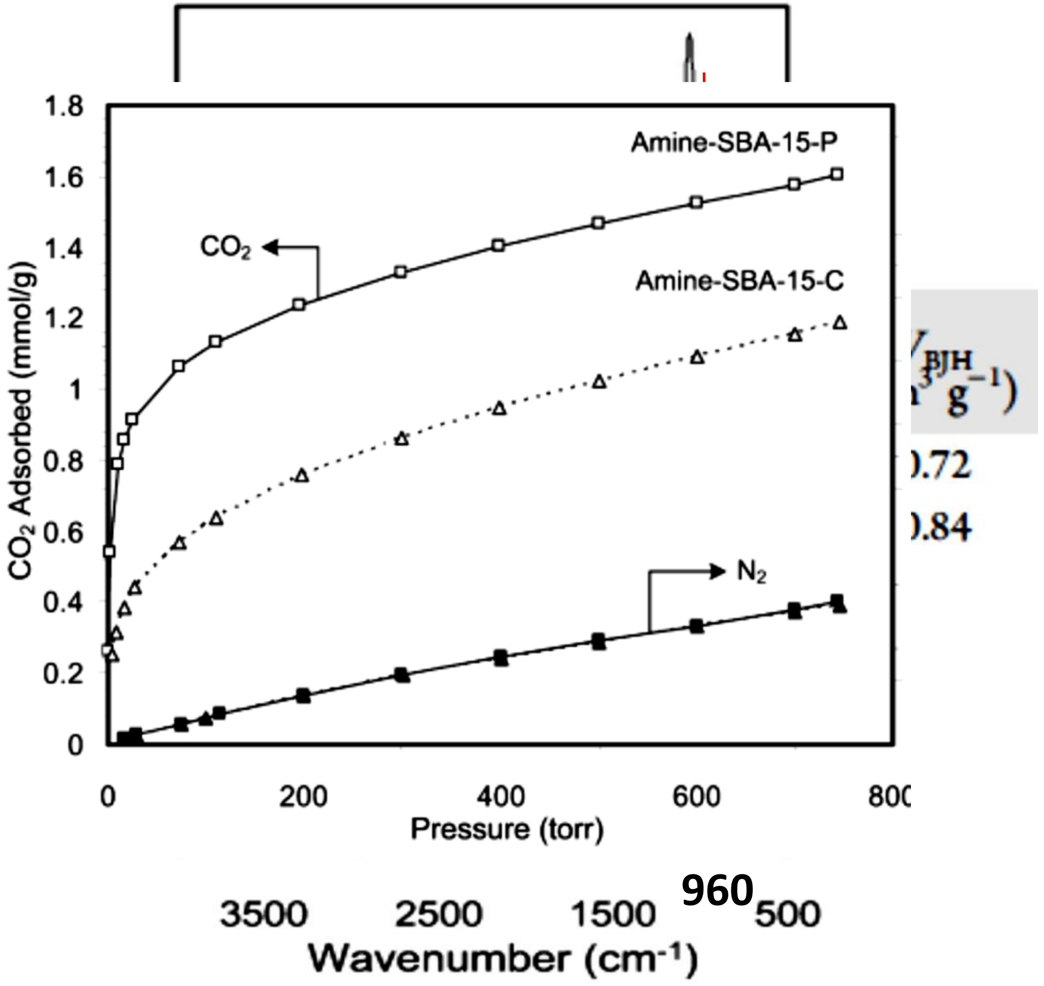
Literature review

➢ **Treatment and Modification by plasma**



Literature review

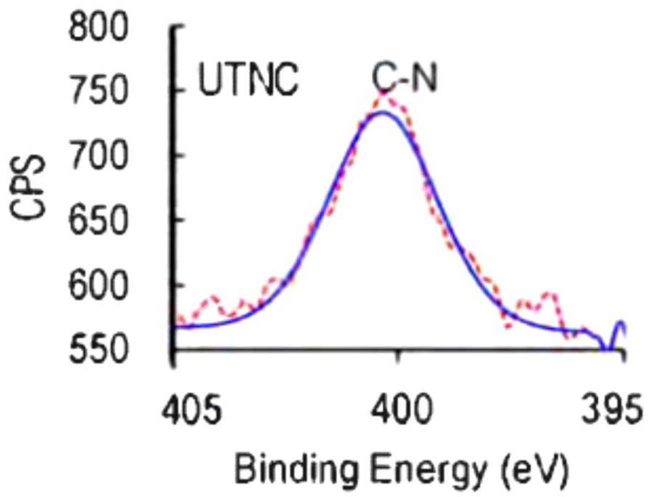
- **Template removal**
  - Min-Hao Yuan,2014, SBA-15 template removal by O2 glow discharge plasma to High Surface Area, High Silanol Density, and Enhanced CO2 Adsorption Capacity.
  - Yuan Liu,2009, MCM-41 template removal using dielectric-barrier discharge (DBD) plasma



Literature review

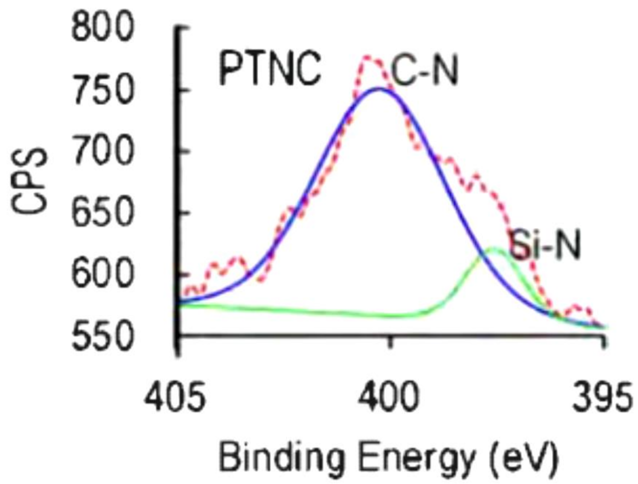
➢ Plasma treatment effect on nanoparticles

- Min-Hao Yuan,2014, SBA-15 treatment to improve chemical interaction between ATPES and silica
- W.Yan,2012,SiO2 NPs treated by non-thermal plasma to disperse uniformly and form strong covalent bond with epoxy polymer matrix



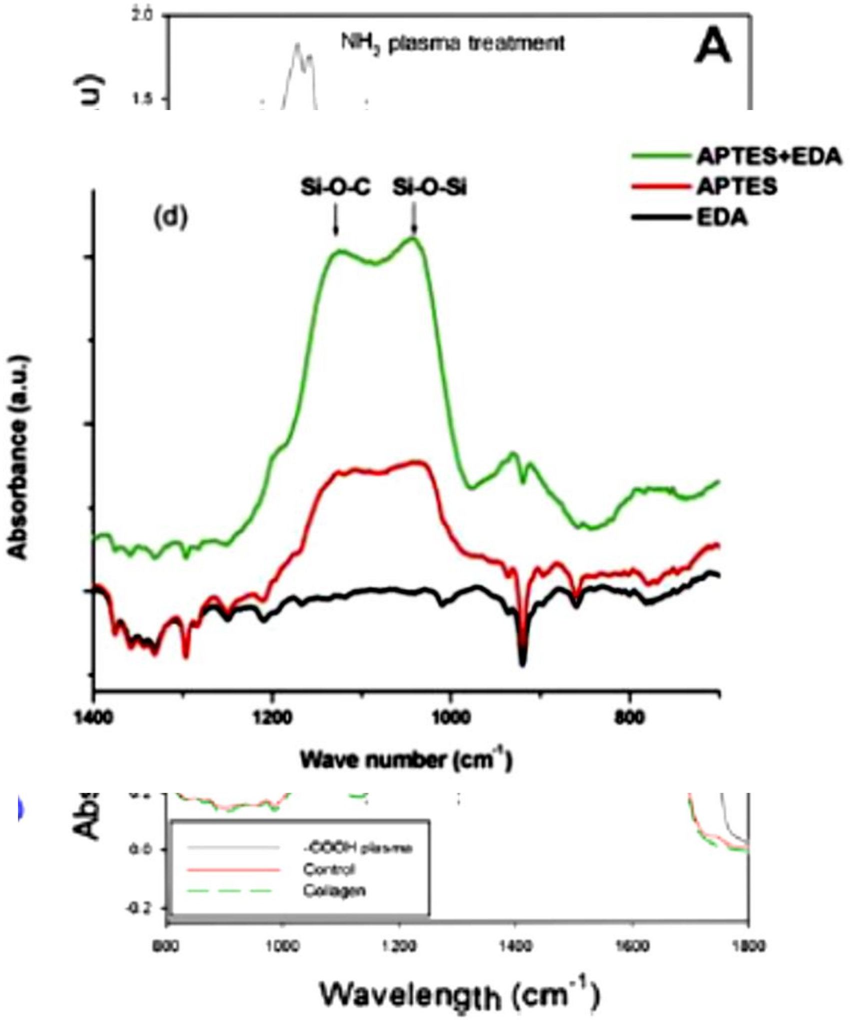
(a)

sample
amine-SBA-15-C
amine-SBA-15-P



Literature review

- Direct surface modification
  - F.Taraballi,2012,Colagen amino and carboxyl functionalization by CO2 and N2/H2 plasma
  - P.Gandhiraman,2009,amine functionalization of cycloolefin by ATPES plasma



Literature review

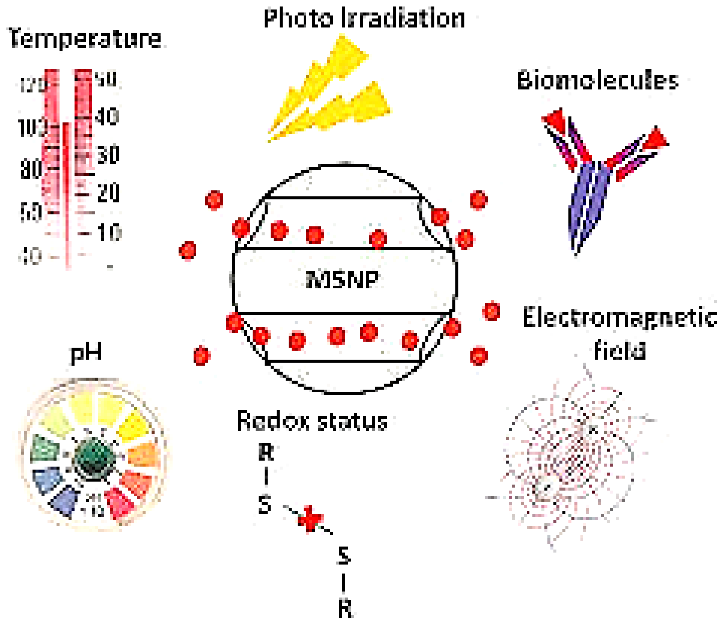
Silica nanoparticles in drug delivery

- ✓ Physicochemical properties
- ✓ Simple surface modification

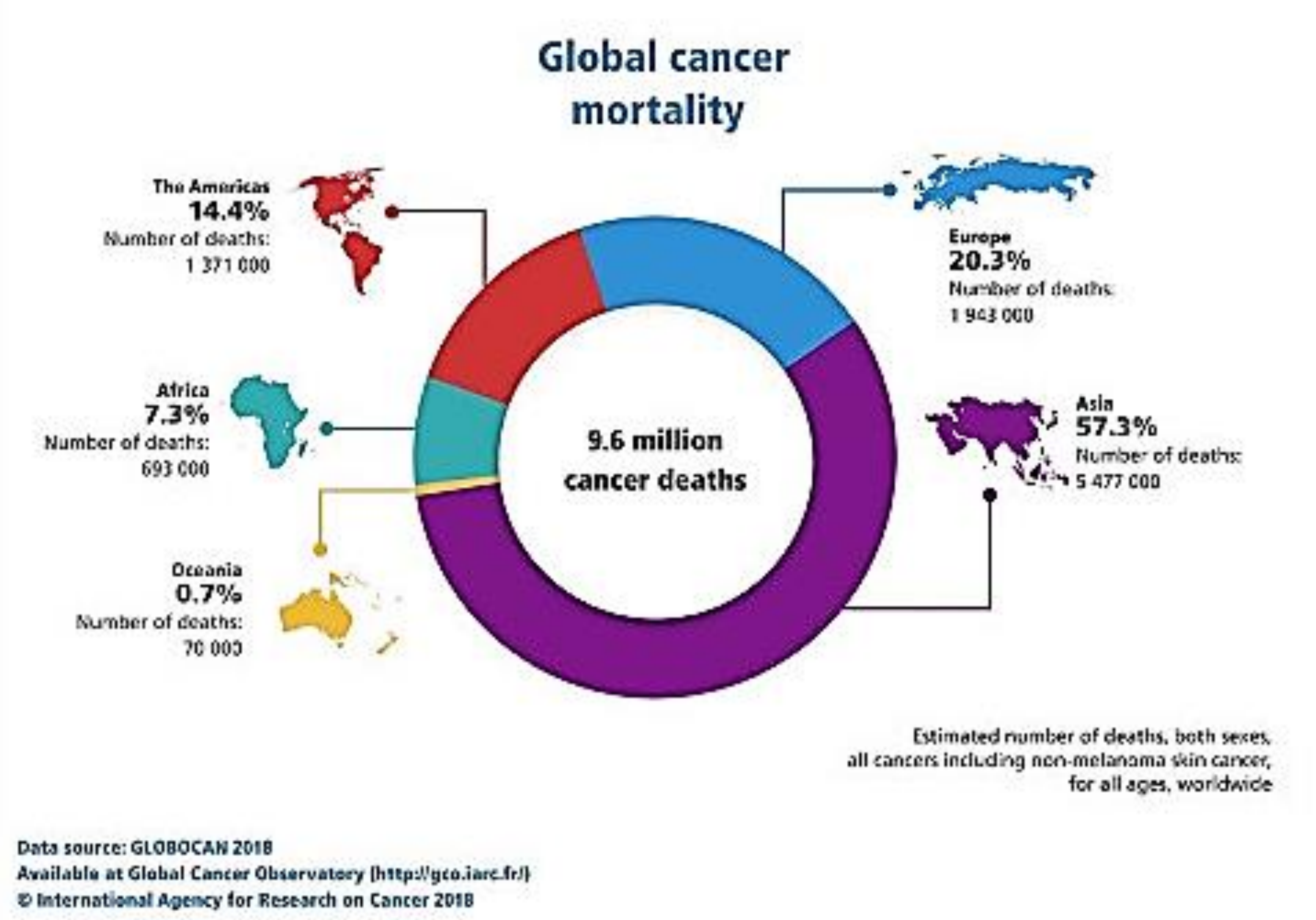
Stimuli	Responsive Linker	Capping Agent
Temperature	Octadecyl (C_{18}) chains	Paraffins
Temperature	PNIPAm	PNIPAm
Electric field	4(3-cyanophenyl)butylene dipolar molecule	-
Magnetic field	Hybridization of 2 ssDNA	γ-Fe_2O_3 NPs
Light	Azobenzene derivatives	β-CDs
pH	Acetal linker	Au NPs
pH	Boronate ester	Fe_3O_4 NPs
pH	Benzoic-imine bonds	Polypseudorotaxanes
Redox potential	–S–S–	ssDNA
Redox potential	–S–S–	PEG
Enzymes	MMP-degradable gelatin	Gelatin coating
Enzymes	β-galactosidase-cleavable oligosaccharide	β-galacto-oligosaccharide

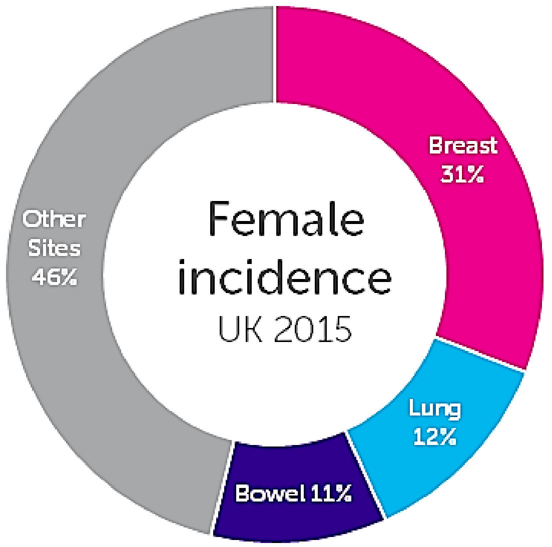
Motivation

- **MSN**s have Unique structure and surface properties .
- **Cereal husks** are a excellent Biosources for MSNs synthesis and It is amazing to synthesis a valuable material from Bio waste.
- **It** is very interesting to use interdisciplinary science such as **plasma** to increase the efficiency of drug delivery systems.



Motivation


Global cancer mortality
The Americas
14.4%
Number of deaths:
1 371 000
Europe
20.3%
Number of deaths:
1 943 000
Africa
7.3%
Number of deaths:
693 000
9.6 million cancer deaths
Asia
57.3%
Number of deaths:
5 477 000
Oceania
0.7%
Number of deaths:
70 000
Estimated number of deaths, both sexes, all cancers including non-melanoma skin cancer, for all ages, worldwide
Data source: GLOBOCAN 2018
Available at Global Cancer Observatory (http://gco.iarc.fr/)
© International Agency for Research on Cancer 2018


Female incidence
UK 2015
Breast 31%
Lung 12%
Bowel 11%
Other Sites 46%

Research Gap

Mesoporous silica nanoparticles can green synthesis from cereal husks, while their properties are not investigate in drug delivery systems

Effect of plasma on structure, physicochemical properties and modification of Mesoporous silica nanoparticles as nano-carrier are not investigate.

In-Vitro and In-Vivo cytotoxicity of Mesoporous silica nanoparticles with cereal biosource and plasma modified are not investigate.

Thesis Objectives

- Bio-silica extraction from cereals husk such as rice husk and wheat husk.
- Synthesis mesoporous silica nanoparticles from bio-silica precursor.
- Increase loading capacity to improve drug delivery ability.
- Investigation on effect of plasma on structure and physicochemical properties of nanoparticles.
- Surface modification of nanoparticles by glow discharge plasma.
- Investigation on drug delivery behavior of synthesized nanoparticles and evaluation drug loading and release profile.
- Evaluation in-vitro and in-vivo cytotoxicity of synthesized nanoparticles

Research Methodology

Literature review

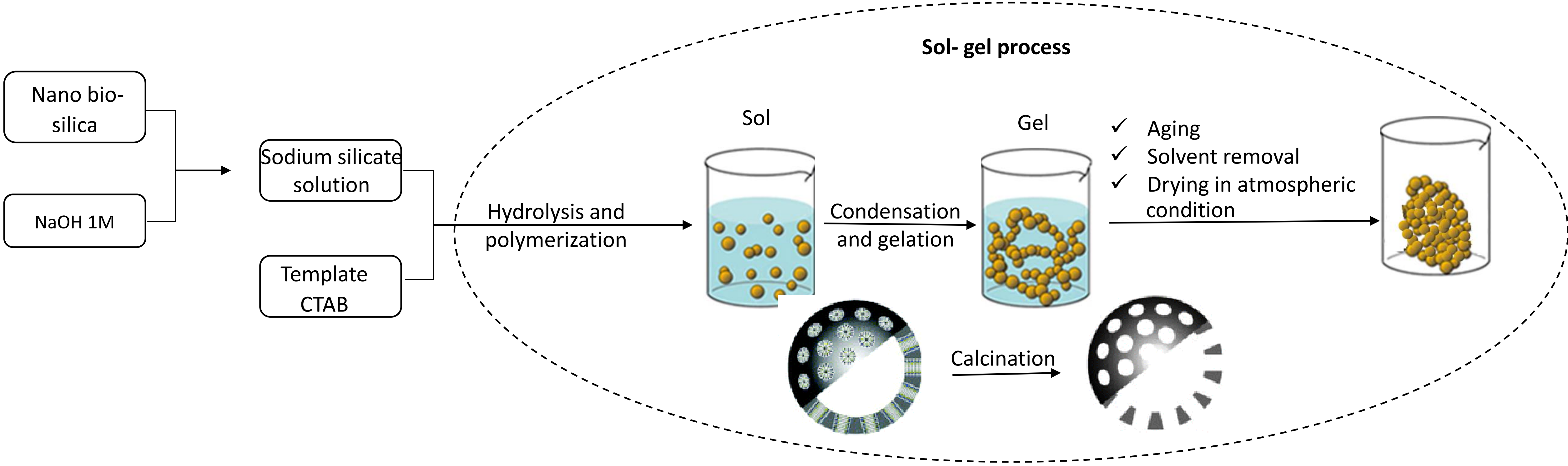
- Bio-silica from cereal husks
- Mesoporous silica nanoparticles
- Surface modification by plasma

Research Methodology

Bio-silica extraction from cereal husks

Research Methodology

➢ **Sol-Gel process to synthesis MSNs**

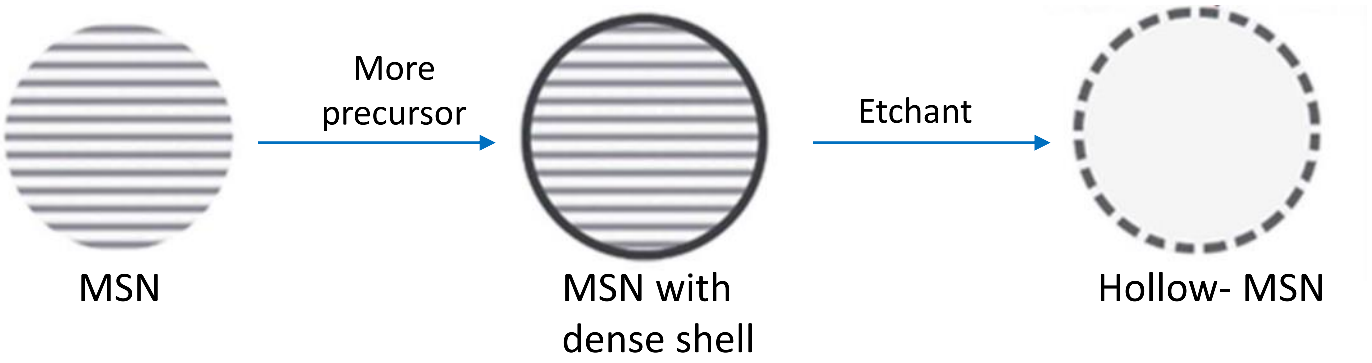


Introduction

➢ Increase drug loading efficiency

→ Selective dissolution strategy

that dissolution of porous core starts from multiple nucleation sites, these small dissolved sites become larger overtime and interconnected with each other until complete core dissolution.



MSN modification by glow discharge plasma in drug delivery

- To compare physicochemical properties of NPs before and after plasma treatment
- To investigate the effect of plasma treatment on drug loading and release behavior
- To compare the effect of plasma on functionalization of MSNs between treated and untreated cases
- Direct surface modification by functional agents such as ATPES (the feed of reactor is functional agent)

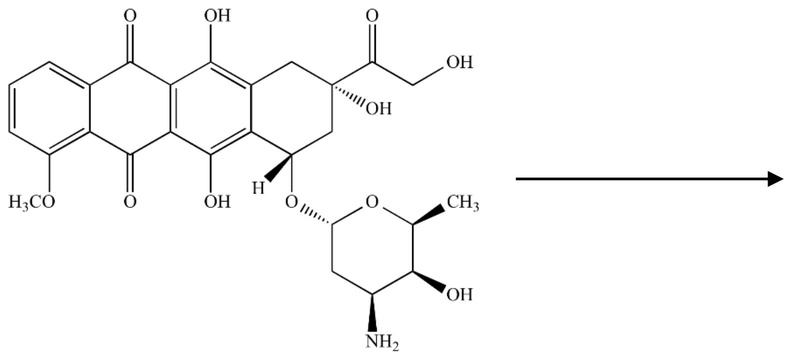
Research Methodology

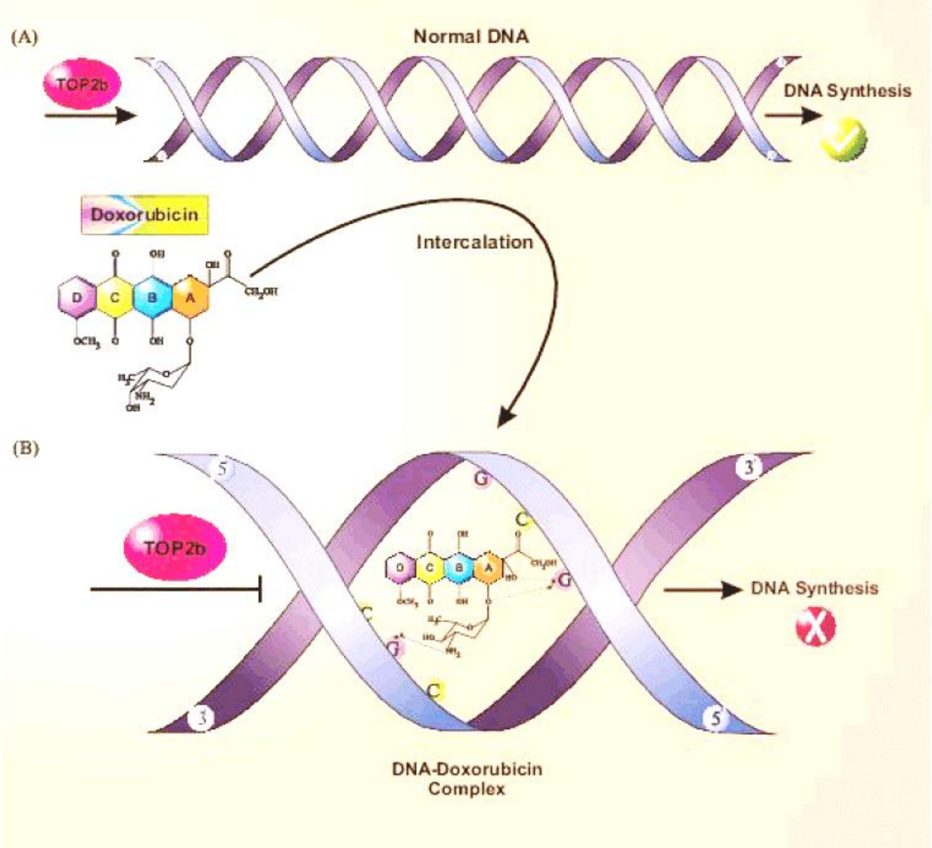
➢ **Characterizations**

No.	Analysis
1	SEM, EDX
2	FTIR Spectrometer
3	TGA
4	BET
5	XRD
6	PORE VOLUME
7	TEM

Research Methodology

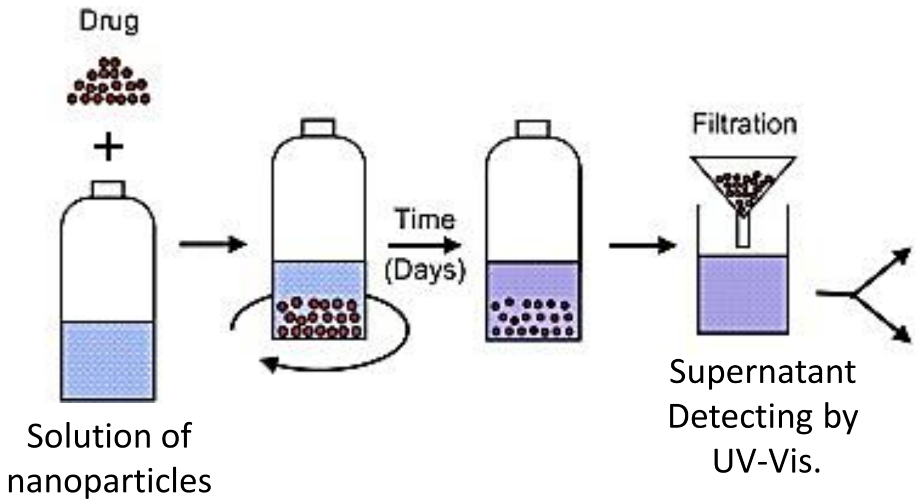
- **Drug delivery studies**
  - Doxorubicin





Research Methodology

- **Drug delivery studies**
    - Doxorubicin loading and release analysis



$$EE\ (\%) = \frac{\text{Amount of drug added} - \text{Amount of drug in supernate}}{\text{Amount of drug added}} \times 100$$

$$DL\ (\%) = \frac{\text{Amount of drug added} - \text{Amount of drug in supernate}}{\text{Amount of nanoparticle}} \times 100$$

Research Methodology

- **Drug delivery studies**
  - Doxorubicin release analysis
  - Release profile detecting for 24 hours at pH 7.4 ,6.5 and 5.5 and Temperature 37°C and 42°C

→

→

Amount of drug release detect by UV-Vis

Research Methodology

➢ Cytotoxicity Analysis

- ➢ MTT assay on MCF-7 cell line as a model cancerous cell and HFF-2 cell line a model body cell.
- ➢ In-vivo cytotoxicity analyses on BALB/c mice at diffirent nanoparticle concentration.

Time Table

No.	Activity	Time needed (month)
1	Literature review	2
2	Buy supplies and materials	2
3	Synthesis and modification	3
4	Characterization	5
5	Performance test	5
6	Final experiments and thesis writing	2

Thanks for your attention

Table 1.1 Composition of RHA derived from calcination of raw RH at 600 °C for 12 h.[29]

SiO_2	Al_2O_3	Fe_2O_3	CaO	MgO	K_2O	Na_2O	MnO	TiO_2	P_2O_5
93.2	0.13	0.07	1.23	0.25	0.78	0.08	0.33	0.006	0.15