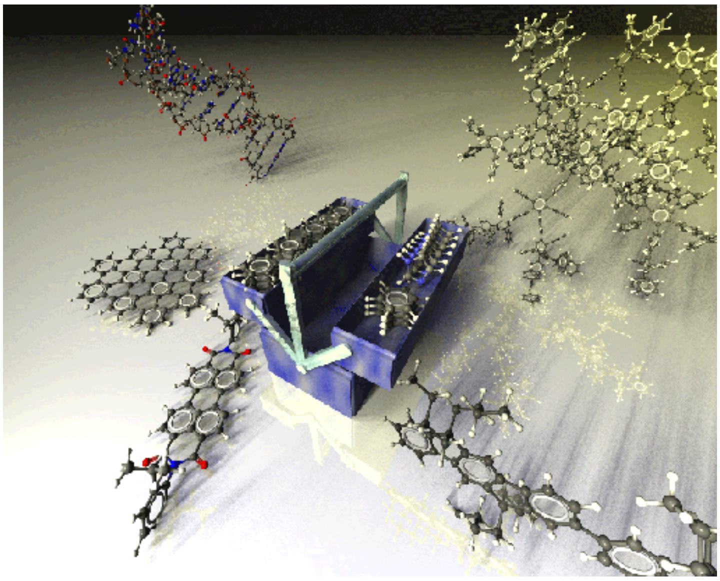
RESEARCH PROJECTS



PROJECT TITLE: Synthesis of New Phthalocyanine Derivatives for Photodynamic Therapy
PROJECT NUMBER: GYTE 2007-A-1
PROJECT TIME: 2007-2009

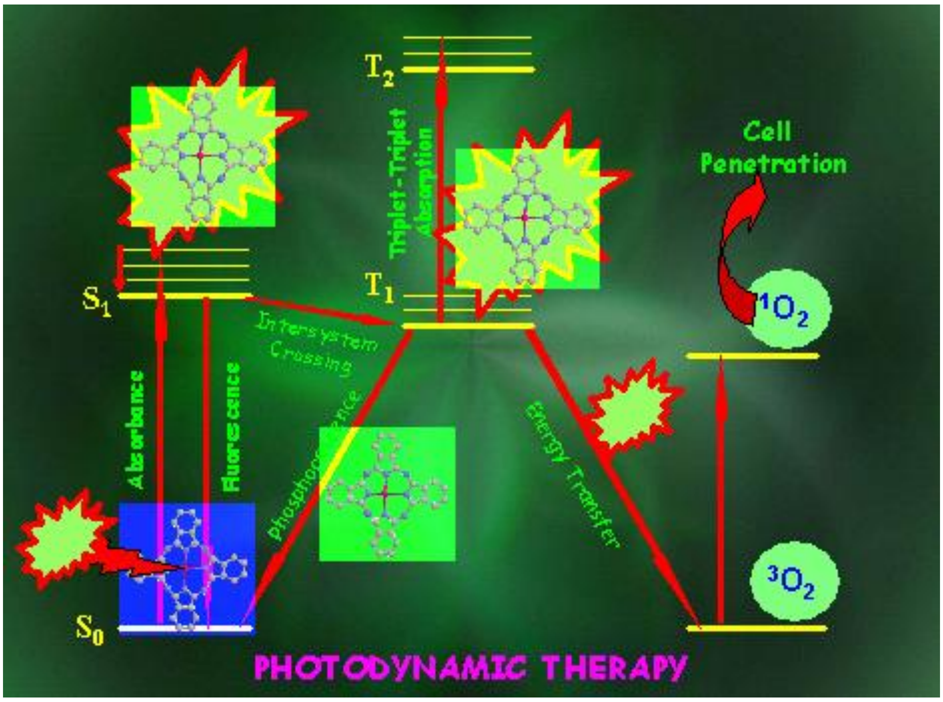
ABSTRACT

Phthalocyanines and metallophthalocyanines have been studied in great deal for many years, mostly in terms of their uses as dyes and catalysts. Recently, they have also found applications in many fields in materials science, especially in nonlinear optical(NLO) devices, liquid crystals, Langmuir-Blodgett films, electrochromic devices, gas sensors, and photosensitizers for photodynamic therapy of cancer.

Some water-soluble phthalocyanine compounds have potentially for use as photosensitizers in photodynamic therapy (PDT) since they can be injected

directly into the bloodstream. The water solubility of these photosensitizers is an additional advantage.

The aim of our ongoing research is to synthesize water-soluble phthalocyanines to be used as potential PDT agents. Herein, we will study the synthesis, characterization and spectroscopic properties of 2-mercaptopyridine substituted Zinc, Aluminum, Gallium and Indium phthalocyanine derivatives. We also study photophysical and photochemical properties of these compounds.



PROJECT TITLE: Synthesis and Photodynamic Therapy Applications of Phthalocyanine-Nanoparticle Photosensitizers
PROJECT NUMBER: TUBITAK TBAG-107T832
PROJECT TIME: 2008-2010

ABSTRACT

Phthalocyanines have attracted much attention because of their applications as pigment and catalysis in the past decades. In recent years, phthalocyanines have found applications in the area of materials science especially in nonlinear optic equipments, liquid-crystals, Langmuir-Blodget films, electro chromic equipments, gas sensors, and as photosensitizer in the cancer treatment with photodynamic therapy (PDT).

Their absorption in the high wavelength (Near IR), high quantum yield, high triplet time and effective oxygen produce capacity lead phthalocyanines to have potential applications in photodynamic cancer therapy. There are several studies in the photodynamic properties of phthalocyanines. In addition, Photosens® which is phthalocyanine compound, is using in the cancer treatment with photodynamic therapy.

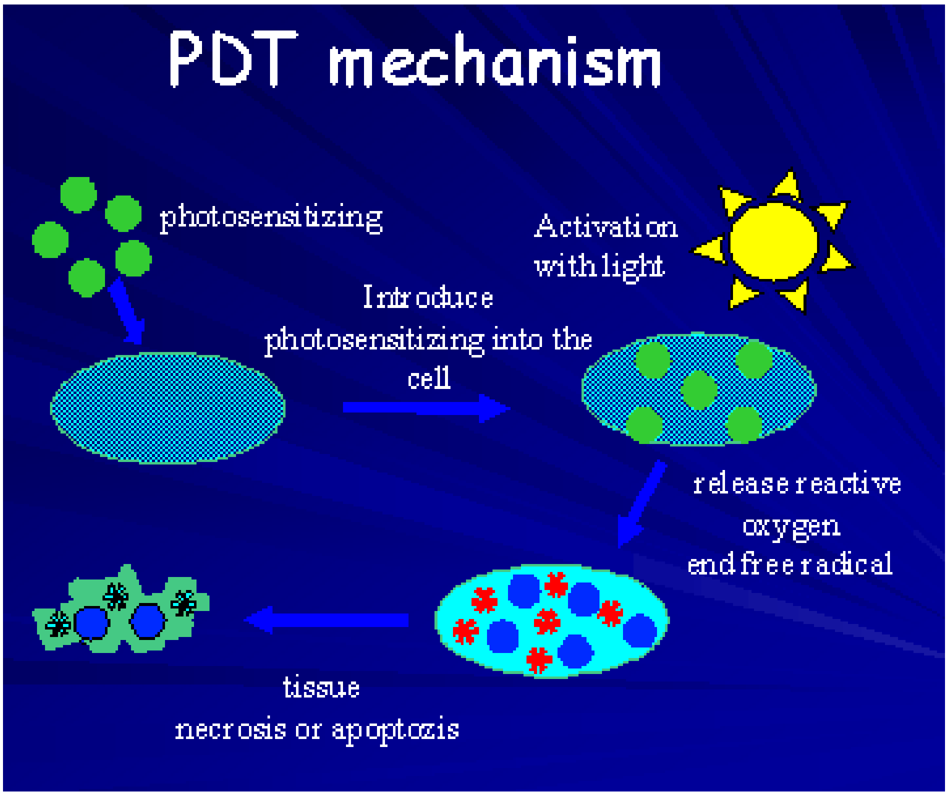
Water-soluble photosensitizers have great advantages in the photodynamic therapy because they can inject directly to body-liquid. However, water solubility is not sufficient for an ideal photosensitization. Photosensitizer molecules must also dissolve in the organic solvents to pass on the cell-membrane. Finally, an ideal photosensitizer must be soluble in both water and

organic solvents. Water-soluble phthalocyanines can be obtained by substution of several groups to phthalocyanine ring.

The aim of this project is the synthesis of phthalocyanines compounds which are soluble in both water and organic solvents as photodynamic therapy agents. Two major handicap in the application of phthalocyanines as photosensitizer are; (i) the solubility problem and (ii) the aggregation in the solvents. In this study, the solubility problem will be solved by attaching of substituents which increase the solubility and aggregation will be prevented by using axial ligands. For this reason, metal atoms which are capable to chelate with axial ligands such as aluminium, gallium, and indium will be used. After the characterization of synthesized new compounds, their spectroscopic, photophysical and photochemical properties will be investigated for their potential applications in cancer photodynamic therapy.

And then, the activity of these phthalocyanine compounds will be increased by mixing with semiconductor CdTe nanoparticles which will be synthesized during this project. After these investigations, cell experiments will be done by our Biologist group.

One can expect that the synthesis of phthalocyanine derivatives which are soluble in both water and organic solvents and their combination with semiconductor quantum nanoparticles will be milestone in the cancer photodynamic theraphy.


PDT mechanism
photosensitizing
Activation
with light
Introduce
photosensitizing into the
cell
release reactive
oxygen
end free radical
tissue
necrosis or apoptozis

ROJECT TITLE: Synthesis of Novel Phthalocyanines as Photosensitizer and Their applications for Photodynamic Therapy *in vitro*
PROJECT NUMBER: Career Project-104T217
PROJECT TIME: 2005-2008

ABSTRACT

Photodynamic therapy (PDT) is a minimally invasive treatment with great promise in malignant disease. It can be applied before, or after, chemotherapy, ionising radiation, or surgery, without compromising these treatments or being compromised itself. The procedure requires exposure of cells or tissues to a photosensitizing drug followed by irradiation with visible light of the appropriate wavelength, usually in the red or near-infrared region and compatible with the absorption spectrum of the drug. Upon light absorption, the photosensitizer undergoes excitation that brings it in its excited triplet state. The triplet can participate in a one-electron oxidoreduction (Type I photochemistry) with a neighboring molecule, producing free radical intermediates that can react with oxygen to generate various reactive oxygen species (ROS). Alternatively, the triplet-state photosensitizer can transfer energy to ground state oxygen (Type II photochemistry),generating singlet molecular oxygen, a highly reactive form of oxygen that reacts with many biological molecules, including lipids, proteins, and nucleic acids.

The first drug approved by several agencies for PDT is a porphyrin oligomer (Photofrin), which is highly effective but exhibits several drawbacks. Therefore, in recent years have developed like phthalocyanines (Pcs) many second-generation new photosensitizers.

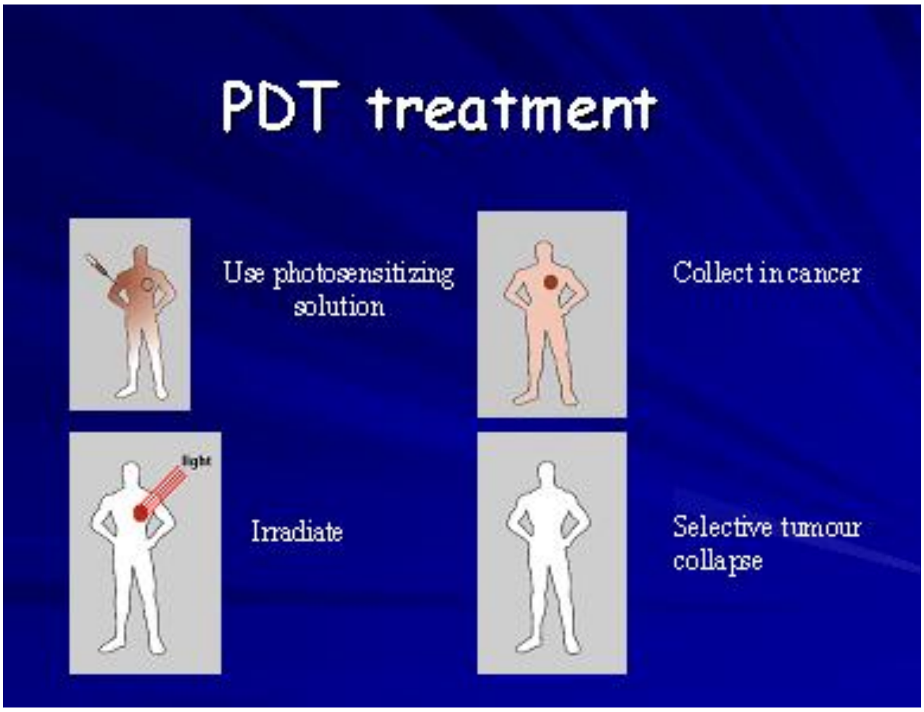
It is found that phthalocyanines are better photosensitizers for PDT than others, such as porphyrins, naphthalocyanines, etc. Pcs exhibit effective cell penetration because of their chemical stability, photodynamic activity, and proper light absorption region.

Various Phthalocyanines are being synthesized in our Chemistry Department. Due to their excellent photochemical properties and potential photosensitizers for the photodynamic therapy, we want to focus in this project on Phthalocyanines and their cellular responses.

For this purpose, the effect of the newly-synthesized mono-and bis phthalocyanines including through thia briged alkyl and polyoxethylene side chains, on cell death especially on apoptosis and related death molecules will be investigated in various cancer cell lines.

Recently,the role of apoptosis in the treatment of cancer becomes clearer. Defects in apoptosis contribute to resistance to cancer therapies and signalling through the death receptor pathways, contributes to sensitivity of cancer cells towards cytotoxic treatment. Molecular insights into regulation of apoptosis and defects in apoptosis signalling in cancer cells will provide novel approaches to define sensitivity or resistance of cancer cells towards anticancer therapy.

Finding a suitable photosensitizer that triggers apoptosis will allow for a better selection of treatment regimens with the goal of avoiding ineffective treatment regimens for PDT.


PDT treatment
Use photosensitizing solution
Collect in cancer
light
Irradiate
Selective tumour collapse

PROJECT TITLE: Mesomorphic molecular materials for electronics: structural organization on the substrate surface, TUBITAK, 108M384, (2009-2011)
PROJECT NUMBER: TURKEY-RUSSIA Bilateral Project-108M384
PROJECT TIME: 2009-2011

Highly π-conjugated organic systems such as phthalocyanines (Pc) exhibit unique electrical and nonlinear optical properties that can be modulated taking advantage of their capability to form stable complexes with metal ions. The self-assembling of two or more of these macrocyclic units in one-dimensional arrays can lead to molecular materials with improved physicochemical characteristics. Thus, peripheral and non-peripheral substitution of the phthalocyanine core with long flexible hydrocarbon chains provides these compounds with thermotropic liquid-crystalline behavior showing discotic mesophases in which the macrocycles are stacked up, giving columnar structures surrounded by the hydrocarbon chains. Much interest has been expressed in conductivity and optoelectronic properties of phthalocyanine films.

Many soluble Pcs exhibit a columnar mesophase and heating the film above the crystal-mesophase transition can improve the long-range ordering of the film without destroying its homogeneity. The combination of spin-coating technology with mesomorphic ordering can produce highly ordered and uniform films. The flat disc-like shape of the molecules favors intermolecular interaction leading to the formation of aggregates in the form of columnar stacks. These properties have awakened interest in the study of the relationship between physical properties of phthalocyanine films and molecular orientation.

This project is to solve the fundamental problem of study of the nature of self-organization phenomena in the complex molecular system on the substrate surface and the influence of macroparameters in the finite structure.

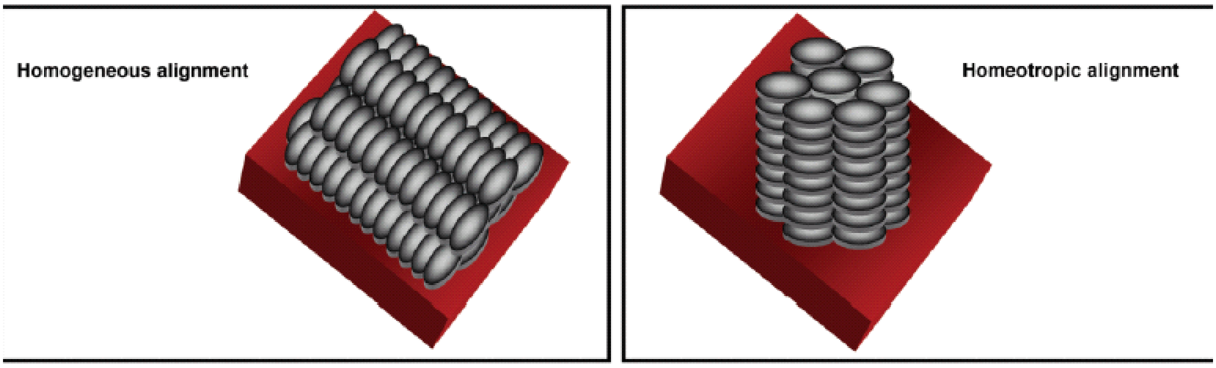
To reach the main aim of the proposal the following objectives will be solved:

1) Design of the liquid crystalline phthalocyanine compounds
2) Developing improved synthetic methods through new and more selective chemical reactions leading to higher yield and more pure compounds
3) Structural characterization of the compounds.
4) Mesophase characterization of the LC compounds.
5) Study of the influence of the molecular structure of Pcs on the films alignment and ordering;
6) Study of the influence of the external factors (substrate material and roughness, regimes of heating and cooling, magnetic field)
7) Preparation of phthalocyanine films with controlled and reproducible alignment and ordering study the relationship between film alignment and their electrical properties.

Novel peripheral, non-peripheral octa and tetra- S and O atoms containing alkyl and poly(oxyethylene) substituted liquid crystalline lead and copper phthalocyanines will be chosen as test subjects. In the synthesis of phthalocyanines, microwave and classical synthesis methods will be used to improve the reaction yield and selected the most yielded method. Mesomorphic properties of these Pc complexes will be investigated for determination of the substitution effects such as octa, tetra, peripheral and non-peripheral on mesomorphic behaviour of these complexes.

The orientation of phthalocyanine columns in thick (a few micrometers) and in thin films (a few tens of nanometers) and the influence of confinement in the type of the alignment will be studied using X-ray, polarized absorption spectroscopy and advanced characterization techniques based on polarized Raman and IR spectroscopy. The orientation of the columns in those films will be characterized as a function of the preparation method, the polarity and roughness of the substrate and the number of LC-solid interfaces (one or two).

On the basis of the analysis of experimental results the phthalocyanines forming the films with homogeneous alignment of columns, which is necessary for field-effect transistors, and phthalocyanines forming the films with homeotropic orientation of columns, required for photovoltaic cells and light-emitting diodes will be chosen. The main factors determining the type of alignment which are necessary to control the adequate alignment of columns between electrodes will be established.



PROJECT TITLE: Synthesis, photophysical and photochemical properties of novel type photosensitizers for photodynamic therapy, TUBITAK, 111T066, (2011-2013)

PROJECT NUMBER: TBAG-111T066

PROJECT TIME: 2011-2013

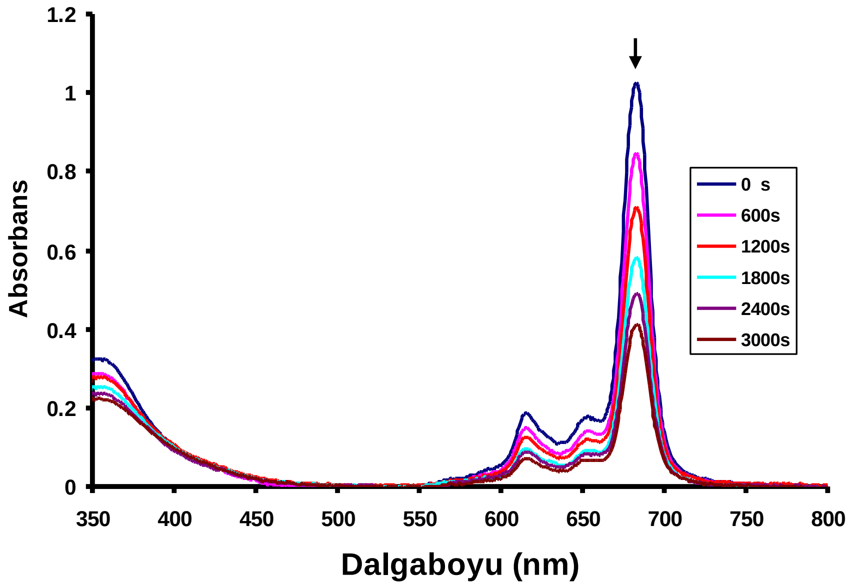
Phthalocyanine (Pc) compounds are ideal molecules in order to use in photodynamic therapy (PDT) for cancer treatment due to their special properties such as absorbing in long wavelength (near IR), having high triplet quantum yields and long triplet lifetime and capability of efficiently singlet oxygen generation. For example, Photosens® which is a phthalocyanine compound is used in PDT for cancer treatment in the clinical trials.

Borondipyrromethene, which is more commonly known as BODIPY, has been used in order to determine the biomolecules via fluorescent for a long while. Recently, because the usability of BODIPY derivates has emerged in various fields, these compounds attract all interest onto themselves. BODIPY derivates are studied in a large implementing area such as chemical sensors, logic gates, light-harvesting systems, energy transfer systems and photosensitisers in PDT. Especially, because of their high fluorescent quantum yields, it is pretty easy to pursue them in the human body.

In the phase of treatment, because water soluble photosensitisers can be directly injected into blood, they provide a lot of advantages. However, water solubility is not competent for an ideal photosensitiser. Photosensitiser molecules must be soluble in organic solvents to cross over cell membrane contained lipid. As a result, an ideal photosensitiser must have capability of solubility in both water and organic solvents. It is possible to synthesis photosensitisers which are soluble in both water and organic solvents by adding some moieties on either phthalocyanine or BODIPY.

There are two obstacles which prevent phthalocyanines using in PDT that are problem of solubility and forming aggregation of phthalocyanine compounds. In this project, the solubility problem will be removed by adding water soluble BODIPY derivates on the phthalocyanine macrocycle and this increases solubility of these photosensitisers in water. In addition, because the BODIPY derivates selected are bulky groups, intermolecular interactions will be minimized that enables to reduce the aggregation. The most important problem of using BODIPY derivatives' in PDT is to absorb in shorter wavelength, when it is compared with an ideal photosensitiser. In order to remove this problem, it is planned to obtain BODIPY derivates by adding of these derivatives to phthalocyanine framework that enables these compounds absorb longer wavelength. The purpose of this project is to synthesis the phthalocyanine compounds substituted with water soluble BODIPY groups which will be used as PDT agents. In the project, it is aimed to obtain ideal PDT agents by integrating phthalocyanine with BODIPY on a single molecule and also by bringing together the advantages of both molecules. Zinc metal will be use as central metal atom which is most using central metal atom for PDT applications of phthalocyanine compounds. After the characterisation and investigation of spectral properties of new compounds, in order to emerge the usability of them in PDT, the photochemical and photopysical properties of these compounds will be studied.

Through this project, phthalocyanine and BODIPY compounds which form the two considerable classes of inorganic and organic chemistry will be brought together on a single molecule and it will be the first time that the features of new compounds will be studied for PDT. It is thought that the new sorts of photosensitisers formed by integrating these two classes of photosensitisers will be the turning point in PDT for cancer treatment.



PROJECT TITLE: Single-walled carbon nanotube/phthalocyanine hybrid materials: preparation, characterization and sensing properties, TUBITAK, 111M699, (2012-2014)

PROJECT NUMBER: TURKEY-RUSSIA Bilateral Project-111M699

PROJECT TIME: 2012-2014

In order to satisfy the demands of the rapid development of nanotechnology, it is necessary to develop different kind of functional material possessing electrical, optical, or mechanical properties. Amongst these, the hybrid materials play more and more important roles in these new technologies, due to their synergetic combination of two or more components. A flourishing area of the pertaining research is focused on the smart integration of carbon nanotubes (CNT) with phthalocyanine (Pc) complexes for enhancing optoelectronic, electro-catalysis and sensing properties. The results have shown that these hybrids are expected to be more efficient in improving the relative responses compared to the individual CNT or Pc species.

Pc, as organic molecules consisting of a planar π-conjugated skeleton with a metal at the centre, have attracted interest for sensing applications due to the following advantages. These advantages:

(1) an exceptional thermal and chemical stability compared with most of molecular materials.
(2) a versatile chemical system, leading to a vast amount of compounds with modulated properties through varying substituents on the ring.
(3) an excellent processability, resulting in the accomplishment of a large variety of thin films by different deposition methods.

Although the Pc-based sensors have been studied for decades, there are still several critical limitations which need to be overcome. these include:

(1) the improvement of the reproducibility of the organic thin film sensors due to the difficult control of the crystalline orientation of the polycrystalline film of Pc.
(2) the improvement of the selectivity of the Pc thin film sensors.
(3) miniature, portable, robust, energy saving and low cost devices need to be fabricated, in order to satisfy the rapid development of nano-sensors together with several other kinds of particular applications.

CNTs on the other hand, discovered by Ijima in 1991, which can be considered as another promising candidate for sensor applications, have aroused considerable interest due to their unique electronic, metallic and structural characteristics. In particular single-walled carbon nanotubes (SWNT), having their special quasi-one-dimensional electronic structures and structure dependent metallic character, as well as their extremely high surface area, provide excellent grounds for unique sensing systems. Several types of devices which were based on the use of SWNTs have been found to be sensitive to various gases as well as other chemical analytes, such as ammonia, ethanol vapor, NO_2, CO, CH_4, dimethylaminoethanethiol, dimethyl methylphosphonate, etc. Furthermore, the excellent electrical conductivity, large surface area, significant mechanical strength, surface chemical reactivity and pore structure make CNTs attractive materials for electroanalysis. Although semi-conducting pristine SWNTs have been proved to be good sensing materials for detecting some molecules, the development of SWNT based gas sensors is hampered by the shortcomings of pristine SWNTs in practical applications; for instance the processability (easily aggregated) of pristine SWNTs imposes limitation on analytes detection. Functionalization of SWNTs has been implemented widely to tackle these restrictions, including attaching sensing groups, coupled to conducting polymers, metals and metal oxides. The development of nanotube-organic composites is proving to be a promising approach to feasibly incorporating carbon nanotubes into devices of designed synergetic functions. For this reason, hybrid molecular systems based on conjugated organic molecules and carbon nanotubes are receiving considerable interest.

The functionalization of SWNTs with Pc derivatives is a great challenge to fulfill in order to satisfy all of the above requirements. Two general approaches for the functionalization of SWNTs have been reported: the covalent attachment of molecules to the open edges or sidewalls of SWNTs and the noncovalent interactions of aromatic molecules or macromolecules to the outer nanotube walls. In principle, the noncovalent functionalization is particularly attractive since the electronic structure of the nanotubes remains essentially unaffected.

Recent studies have proved that the alignment of CNTs plays a critical role in the properties of nanotube based materials. However, processing materials with well-controlled CNT alignment still remains a challenge.

There has been growing interest in the field of dispersion of CNTs in both thermotropic and lyotropic liquid crystal (LC) phases to obtain the ordered structures. These few works demonstrate that liquid crystals act as tunable solvents for the dispersion of nanomaterials, and being anisotropic media, they provide a very good support for the self-assembly of nanomaterials into larger organized structures in multiple dimensions. However, from these scattered results, no obvious correlation seems to exist between the molecular architecture of the building blocks of discotic LC and the hybrid films alignment.

It is well known that phthalocyanines with long alkyl and polyoxy substituents can form LC phases at room temperature. The insertion (dispersion) of CNTs in the supramolecular order of room-temperature discotic liquid crystalline phthalocyanines may lead to novel materials with interesting properties useful for sensor applications.

The principle aim of the current project is to study the structural and functional properties of SWNT-phthalocyanine hybrids thin films which involve phthalocyanines exhibiting LC behavior at room temperature and to construct a comparative performance study with special focus on their sensor properties.