The scientific project of the Department of Drug Science and Technology covers all aspects of drug discovery ranging from drug design, synthesis and characterization to formulation and clinical pharmacology. This multidisciplinary project is of high relevance for the University of Turin owing to high regional and national impact. It exploits expertise and skills in pharmaceutical chemistry, drug technology, pharmaceutical biology, pharmacology, clinical pharmacology, biochemistry, physiology, organic chemistry, food chemistry, cosmetic and analytical chemistry. Chemical and pharmaceutical industries are involved in the early stages of drug discovery and development and are mainly focused on the design and synthesis of biologically active molecules and on the determination of their in vitro pharmacological properties. The aims of our research also extend to the understanding of the chemical and physical bases of relationships between drug structure and action, as well as the study of their pharmacokinetic behaviour (ADME). Established lines of research in the Department are in the context of multifunctional drug design and research for cardiovascular, anti-inflammatory and anti-tumoural fields. A wide net of collaborations with worldwide universities, research centers and industries, magnify the project potential.

The Department uses *in-silico* simulations at different levels of complexity (eg, quantum-mechanical, mechanical-molecular hybrid QM/MM) applying them to a range of areas, including: prediction of –physico-chemical properties of chemical / pharmaceutical interest, and the conformational analysis, computer-aided drug design, ligand-based and structure-based virtual screening, study of the reaction path in the presence or in the absence of enzymatic catalysis. The scientific program deal with the total synthesis of bioactive compounds and the functionalization of macromolecules and nanostructures as suitable drug carrier. New green technologies involving non conventional energy sources have been developed for synthetic applications and highly efficient plant extraction. Such experience in the design of innovative ultrasonic and microwaves batch and flow-reactors, enabled the access to the FP7 funding as well as to collaborations with lead industrial partners. For this goal the outstanding analytical facilities in the department offer a fundamental support to all the investigations.

The pharmacological skills cover studies on several human diseases in the search of new drug therapies. The *in vitro* and *in vivo* models are focused on:

i) correlation between metabolic alterations and cardio-renal diseases;

ii) diabetes and related cardiovascular risks;

iii) modulation of ischemic cerebrovascular and cardio-renal damage;

iv) correlation between the molecular characteristics of individual tumors and the response to anticancer therapies; the pharmacological efficacy is evaluated in tumor and endothelial cells in both in vitro and in vivo models of cancer progression and angiogenesis;

v) effect of natural extracts on the proliferation and viability of normal and tumor cell;

vi) preclinical studies, employing in vitro and in vivo models, focused on the evaluation of the pharmacokinetics and pharmacodynamics of pharmaceutical formulations delivered in nanoparticles with a special focus on GI absorption and drug delivery in the eyes, CNS and cancer;

vii) biological activity of new pro-drug, pro-inhibitory enzymes and the development of new micellar systems;

viii) properties and efficacy of self-assembling and stable squalene nanoparticles with higher activity of parent drugs in both in vitro and in vivo animal models of cancer and tumor angiotensin

The Department has cutting edge topics including sonodynamic research, based on the study of cavitation generated by ultrasound and/or high-energy shock waves capable of activating sonosensitive substances in cancer therapy. Studies of pharmacogenetics and pharmacogenomics are focused on inter-personal variability in drug response according to both to the genetic background and the toxicology.

Another area of interest of the Department is the neurobehavioral pharmacology and toxicology focuses on specific brain areas, and specifically on:

i) the synaptic and molecular mechanisms underlying cognitive learning and stages of acquisition, consolidation and recall of memory;

ii) the modification of cognitive processes induced by bioactive substances, drug abuse, normal senile decay, under stress, psychiatric disorders and neurodegenerative diseases;
iii) the effectiveness of new therapeutic strategies aimed at remission of neuropsychiatric disorders.
Investigative methods used in the evaluation of brain function *in vivo* include the study of cognitive and emotional skills, by carrying out specific tests: working memory, short-term and long-term memory, motivation and timing behavior, spatial learning, habituation processing, and biological techniques at different levels of complexity including: neuroanatomical injury, intracerebral icv administration, cerebral microdialysis, immunohistochemistry, DNA array, Western Blot and RT-PCR real time.
The study of this specific field also include pharmacology and experimental therapies:
i) physiological and pharmacological activities of the peptides produced by the endocrine-metabolic gene ghrelin (ghrelin and obestatine);
ii) pharmacological interventions on the regeneration of pancreatic beta cells;
iii) experimental aspects of pharmacotherapy of cardiomyopathy and vascular-endothelial dysfunction caused by oxidative stress and diabetes mellitus;
iv) the pharmacological regulation of lipolytic and adipogenetic processes;
v) new drugs in the treatment of visceral obesity.

Another important research line is the development of anticancer drug targeting through carriers in systems consisting of liposomes, nanoparticles (nanospheres and nanocapsules) and molecular conjugates. To improve the tropism towards target cells, such systems are modified by conjugation with polymers and the association with carriers able to recognize antigens and over-expressed receptors on the surface of cancer cells. This approach optimizes the pharmacodynamic and pharmacokinetic properties of anticancer drugs delivered while minimizing the toxic and side effects.
The Department's long standing consolidated experience is to be found in the field of pharmaceutical technology on design, preparation and development of particulate systems in lipid matrices, polymers and proteins for the delivery of hydrophilic and lipophilic active ingredients, with different pharmacological actions and for routes of administration.
Particular interest is given to:
i) the evaluation of chemical and physical parameters of particle systems;
ii) the efficiency of incorporation and the *in vitro* release of active ingredients;
iii) the determination of the toxicity of various cell lines;
iv) the *in vivo* bioavailability on laboratory animals.
v) the production of systems in the lipid matrix (SLN), using innovative techniques patented by the Department.
In addition, technological approaches also include the development of colloidal systems such as emulsions, microemulsions, liposomes, and micelles for the incorporation of drugs and active molecules targeted at the dermo-cosmetics. In recent years a big effort has been done in the development of Galenic preparations, both in a national and international health context, as an effective response to specific needs in local hospitals. This activity includes the preparation of medicines tailored to meet the specific needs of individual patients and the transfer of know-how and implementation in health facilities located in Developing Countries (DCs) laboratories. These studies are structured on the basis of international standards for the preparation of Galenic medicines which allow the tailoring of dose and pharmaceutical forms according to specific endemic diseases and environmental conditions, the cut of costs and employing local staff.
Relevant work includes pharmaceutical biology and food chemistry skills that are turning to the study of new extracts or natural products as food supplements or pharmaceuticals. In particular this research is focused on:

i) the study the composition of biologically active plant extracts or distillates to deal with a bioassay oriented approach;
ii) the extraction, isolation and identification of biologically active substances of plant origin;
iii) quality control, safety, and biological activity of produced by arrays of plant origin;

iv) the development of innovative problem solving techniques related to herbal products.

Several studies in the Department are also turning to the development of new strategies for the profiling of secondary metabolism of specific classes of compounds (metabolite profiling) using the typical approaches of metabolomics and the interactions multitrophic. In this context, food safety and quality are the main issues. They are intended for the quantitative determination of contaminants (xenobiotics - pesticides, EDCs and process contaminants - furan, acrylamide, etc.) in food products, semi-finished products, foods for infants and herbal food supplements by means of innovative and automated analytical approaches.

In the field of food quality research is used the foodomic approach which is multidimensional GC-MS analytical techniques EES-GC-MS, GCxGC-MS, LC-MS and chemometrics bioguided techniques. These techniques are useful for the authentication of the botanical origin and geographical characterization of the impact of technology, using process indicators on the product and on-line monitoring, and the definition of the sensory profile of foods (taste and aroma). Furthermore, additional tests for the characterization of biological activity are in development in both *in vitro* and *in vivo* models. In particular are in development tests for antioxidant, substances of plant origin (also present in food), dietary supplements, and synthetic derivatives.

A well-established expertise in physiology, biophysics and pharmacology of ion channels, voltage-and ligand-gated allow the study of the molecular basis of the mechanism of action of neurotransmitters and drugs on ion channels in excitable cells (neuro-hyppocampal, pancreatic cells, chromaffin cells, cardiac tissue.) The study of the molecular ion channel takes place a at the level of a single protein of an isolated cell and of the entire tissue (brain slice), combining conventional electrophysiological techniques such as patch-clamp with the more advanced Micro-Electrode Arrays (MEA). In this context, the research is aimed to develop new prototypes of planar microelectrodes to measure electrical and electrochemical signals from excitable tissues to perfom drug-screening tests. The project also includes analytical studies for the determination of metals (especially heavy metals) and arsenic in Ayurvedic medicines and phytoalimurgic plant species. Further aims concern the application of nanostructure electrodes built and fine tuned in our laboratories for the determination of mercury and methylmercury in these matrices, and other samples in pharmaceutical and food products. Heavy metal toxicology included cadmium in neuroblastoma *in vivo* models.

The characterization structural / functional enzymes, the determination of the subcellular localization and interactions of enzymes of the same metabolic pathway, engineering, site-directed mutagenesis and expression of recombinant proteins in bacterial cells and yeast are the foundation that characterizes research in the field of biochemistry and molecular biology. Research activities are mainly devoted to the study of new enzyme inhibitor in the post-squalenic phase of sterol synthesis as potential hypocholestorlemic antifungal. Currently this line of research is moving towards:

(i) characterization of murine biochemical models on hereditary disorders of cholesterol metabolism;

(ii) effect of new post-squalenic inhibitors on cancer metastatization and tumor angiogenesis of Hedgehog-dependent tumour cell lines.

The first line of research is being conducted through enzymatic determination of cell lines and murine embryos lacking one of the genes of the demethylation apparatus at C-4 sterol (in collaboration with research groups in Europe and America that provide the biological material). The second line of research uses Hedgehog-dependent cancer cells, in collaboration with the IRCC at Candiolo (Turin) to assess the activity of both intermediates of cholesterol synthesis which are considered toxic for the cascade of Hedgehog protein (obtained with yeast engineered in our laboratories), and new inhibitors designed in collaboration with other international research groups.

The Department has been established as a multicentre facility with laboratories where research activities are held in the area of via Pietro Giuria (n° 9, 11 and 13), c.so Raffaello (n° 30, 31 and 33), and at the Institute for Cancer Research at Candiolo (IRCC) that is to say it uses all facility of the former Faculty of Pharmacy and of the former Institute of Physiology and Clinical Pharmacology where our lecturers already work. Some of the research and all the teaching activities of the degree course in Herbal

Techniques are held at the Savigliano campus. All laboratories of the pharmacy and pharmaceutical chemistry and technology degree courses are temporarily located at the via Quarello University Campus.