By means realizing the research project we hereby propose, we would like to produce new generation, effective pharmaceuticals to cure Candidiasis.

Candidiasis is a fungal infection of which major cause is a genus of yeasts, called Candida. The most common of the Candida genus of the yeasts is Candida Albicans; and Candida Albicans is considered the fourth most popular cause of the infections worldwide. The major source of the Candidiasis are hospitals because the Candida Albicans can easily spread in immunologically compromised patients, whose bodies' defensive (immune) system against illnesses and infections is not working probably. This means that, when these people get Candidiasis, they cannot be cured with the use of an antibiotic because the most well known and widely used antibiotic (Amphotericin B) against Candidiasis has serious side effects on human body. Any side effects caused by a drug in immunologically compromised patients is considered very dangerous and in serious cases it may cause death. On the other hand, the side effects originated from amphotericin B has a close relation with in what dosage it is introduced to a patient. The higher the dosage of the antibiotic is, the more serious side effects occurs with the patients under treatment of Candidiasis.

The amount of antibiotic introduced to a patient suffering from Candidiasis is increasing year by year and the primary cause what makes us to use antibiotics in an in increasing amounts is closely related to a factor called "Multi Drug Resistance (MDR)". MDR occurs when an infectious agent, such as Candida Albicans, develop their own defense mechanisms against antibiotics and become "resistant" to be killed by the drugs we use against them. When this resistance occurs for more than one or more effective antibiotics we normally use, then the infectious agent is said to be "multi drug resistant". In order to fight MDR, the use of antibiotics in increased amounts might be a solution; however as it was explained above, the increased amount of antibiotics means that they will be more toxic to human body and cause more serious side effects than normal. This problem, of course, is much more problematic with immunologically compromised patients due to said reasons.

Finding and effective solution to MDR problem is not really easy. Once an infectious agent acquires resistance to a known drug, it means the same drug will not be as effective as it was before. In the first instance, the solution would require a new drug to be discovered as a cure to the infection, which the infectious agent has never been treated before and has no resistance. However, it is not an easy task to discover new types of antibiotics and might require even few decades to produce a usable drug that will serve as a cure. Nevertheless, a more practical, less costly however still a time consuming solution to MDR is just trying to chemically synthesize a new antibiotic molecularly similar to a known drug (parent); but slightly differs from the parent. In this way, it is expected that the synthesized, novel antibiotic structure will not be rejected due to the MDR (because the infectious agent will not be able to recognize the new drug although it is slightly differ from the parent) but it will be as effective as the original drug.

When all of the above mentioned problems are taken into consideration, it becomes a general consensus that there is general need of new anti-fungal agents, preferably totally differs from the current anti-fungal agents, with a specific mode of action (having a mechanism entirely different from a known drug, such as amphotericin B). The good news is such agents have been already discovered, however they bring different kind of research problems along with their novelty. For instance, one of these new generation anti-fungal agents discovered by our research group (which we shortly call the drug as FMDP) is a very effective, potential drug against Candidiasis. However, entirely new and specific mechanism of FMDP requires it to be delivered directly inside the infectious agents (fungal cells) but this is not possible since FMDP does not bear the molecular specifications to penetrate inside a cell. In order to solve this problem, we have already carried out a 3 decades long research to find out the most molecularly similar analogues of FMDP, which will have the specification to penetrate a cell while maintaining the biological activity of FMDP. However, unfortunately, none of the new FMDP analogues were as effective as FMDP.

Consequently, in our search of an effective method that will enable us to deliver the FMDP directly inside the cell without scarifying its activity, we have found "nano-pharmaceutical" approach quite promising. The approach usually requires the molecules of the active drug to be attached on the surface of a nano-sized solid particle, in a way that it will not cause any irreversible chemical modifications that might cause its original activity to be lost against the infectious agents. Once a proper way of attachment is achieved, it is expected that nano-sized particle carrying the active molecules on its surface will directly go in to the cells of infectious agent and release the molecules inside the cells, enabling them to take action as active drugs to cure the infections.

Idea of nano-pharmaceuticals is a decade old approach to bring in new types of active agents into use, which were once discovered as quite effective and promising future drugs but suffered due to above mentioned problems and have been forgotten until someday a new promising approach will offer a solution. Additionally, the idea was also have been applied to well known and widely used drugs like amphotericin B, offering a solution to get rid of MDR and some of the side effects caused by the drug alone. Here it must be stressed that nano-pharmaceuticals indeed offers a very realistic solutions against MDR since the infectious agents do not have mechanism to develop resistance to a solid particle in a nano-size. Because, the mechanism of cellular internalization and molecular recognition of a nano-size particle differs from the one that works in molecular level when a drug is directly introduced to an infectious agent. However, since the nano-pharmaceuticals approach is only a decade old idea, it requires an intensive research to solve the problems specific to it. For instance, the solid particles itself should not be toxic its target because the increased toxicity will always mean increased side effects, which makes the choice of a nano-particle important.

Taking into account the all above mentioned problems and solutions in search of a new and less toxic drugs against the Candidiasis, we hereby propose a research project concerning the FMDP as a potential active drug in the form of a nano-pharmaceuticals. Since the potential of FMDP is well-proven as a new anti-fungal drug by the 3 decades of research we have carried out, and the only problem of FMDP is being delivered inside the cell of infectious agents as mentioned above, we believe that we can finally make FMDP a real drug by means of using a nano-sized particles to deliver it inside the infectious agent. In order to do this, we have chosen a suitable nano-sized particle, iron oxide, which is known to be none-toxic to humans. Because

iron oxide nano particles already naturally exist in human body. Nevertheless, similar researches carried out before us to offer various nano-pharmaceutical solutions proved that they are safe to use.

In order to use the iron oxide nano particles as nano pharmaceuticals, they must be chemically synthesized. Although various methods have been described in literature to synthesize them, only few of these methods have been found to be promising to form nano-pharmaceuticals as potential drugs. However, the described methods have been successfully adopted with the significant improvements made by our research group and we have already demonstrated that iron oxide nano particles synthesized by us can effectively be delivered directly inside the cells of infectious agents; proving its potential to solve the problems of FMDP that struggles to penetrate into the cells. The results we have obtained proving the existence of nano-sized iron oxide particles inside the cells ensures that we can use these particles to deliver the FMDP inside the cells, which can render the FMDP an alternative anti-fungal drug of the future.