Summary

The thesis entitled **"Design, synthesis, gelation studies and applications of DAP derived low molecular mass fatty acid amides and glycodendrimers"** is divided into five chapters.

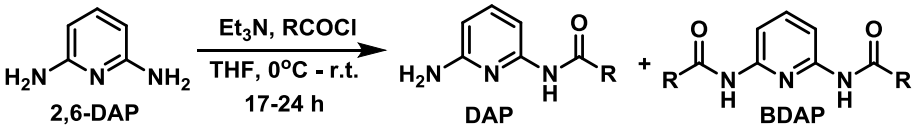
Chapter 1: An Introduction to Low Molecular weight Gels (LMWGs) and their Applications in Drug Delivery

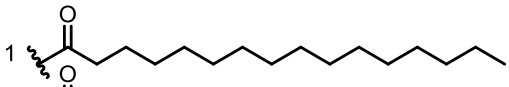
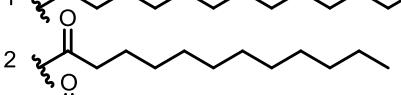
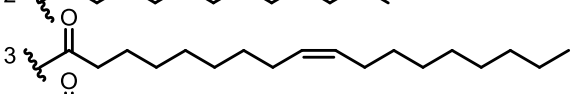
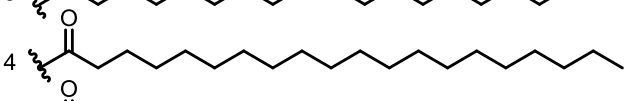
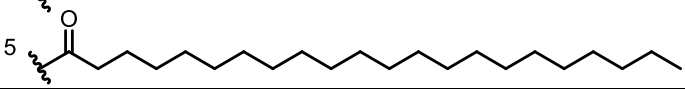
This chapter provides a brief overview about low molecular weight gelators (LMWGs), gels, various types of gels, drug delivery, various drug delivery routes, topical and transdermal drug delivery, and topical and transdermal drug delivery agents (LMWGs and dendrimers). 2,6-Diaminopyridine (2,6-DAP)-derived amphiphiles have emerged as important LMWGs for the construction of various types of gels and acting as good drug delivery agents for topical and transdermal drug delivery applications.

Chapter 2: DAP Derived Fatty Acid Amide Organogelators as Novel Carrier for Drug Incorporation and pH-Responsive Release

This chapter provides a brief sketch about the importance of organogels and bigels. The preparation of organogels and bigels from 2,6-DAP (2,6-diaminopyridine) derived low molecular weight (LMW) fatty acid amide gelators is of great interest due to their applications in drug delivery. This chapter describes the synthesis of a number of DAP derived amphiphiles (**Table 1**) as low molecular weight gelators (LMWGs), their gelation studies and application of the prepared gels as drug delivery agents for topical and transdermal drug delivery.

Table 1: Synthesis of DAP derived fatty acid amides[a]



entry	(R)	time (h)	yield (%)[b] DAP	BDAP
1		24	**16DAP** (81)	**16BDAP** (8)
2		22	**12DAP** (75)	**12BDAP** (10)
3		17	**18UDAP** (79)	**18UBDAP** (trace)
4		20	**20DAP** (87)	–
5		22	**22DAP** (90)	–

[a]Reaction condition: 2,6-DAP (1 mmol), anhyd. Et_3N (2 mmol), RCOCl (1 mmol), anhyd. THF (10 mL); [b]Isolated yield of purified product

To the best of our knowledge, the self-assembling behavior of these amphiphiles was already reported but their gelation behavior has never been reported thus far. Therefore, we proposed to study the challenging gelation behavior of these amphiphiles and application of these prepared gels in topical and transdermal drug delivery.

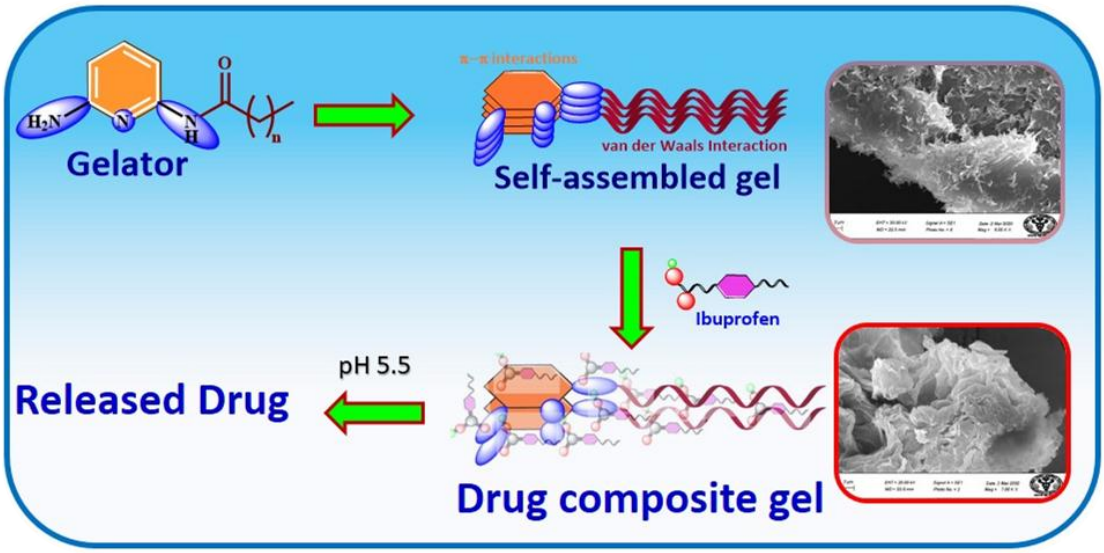


Figure 1. Self-assembling of gelator, drug composite gel and pH responsive release of drug.

Low molecular mass fatty acid amides were synthesized using 2,6-diaminopyridine (DAP) as a linker and alkyl chains of varying lengths, that upon self-assembly form organo- and bigel in various solvent systems. The prepared organogels are able to trap and release ibuprofen drug molecule at room temperature without changing its structure and activity.

This is the first report of DAP derived fatty acid amide organo- and bigelators for drug encapsulation and pH responsive release. The minimum gelation concentration (MGC) of the synthesized organogel is 0.5% w/v which is considered as super gelators. These gels indicated high degree of encapsulation and offer an opportunity in the field of pharmaceuticals to use these analogues as drug carrier vehicles.

Chapter 3: DAP/alginate Based Nanosilver Composite Hybrid Gel Beads for Topical Drug Delivery Applications

To explore the potential of 2,6-DAP derived low molecular weight fatty acid amide gelators in the field of biosciences, herein, we proposed the *in situ* formation of silver nanocomposite gel and two component hybrid gel (LMWG/alginate system) in which alginate network can provide a spherical core to compel LMWG self-assembly as shown in **Figure 2**.

This chapter provides a brief overview about the importance of nanosilver composite gel, hybrid gel and shape controlled hybrid gel beads. The preparation of shape controlled hybrid gel beads is of great interest because of easy handling and can use in bone healing, wound recovering and surgical interventions. This chapter describes the preparation of hybrid gel and hybrid gel beads, and *in situ* formation of AgNPs (silver nano particles) in **22DAP** gel and extended interpenetrating **22DAP**/alginate gel beads (**Figure 3**) for topical application because AgNPs are superior alternative to conventional antibiotics in view of unique mechanisms of action.

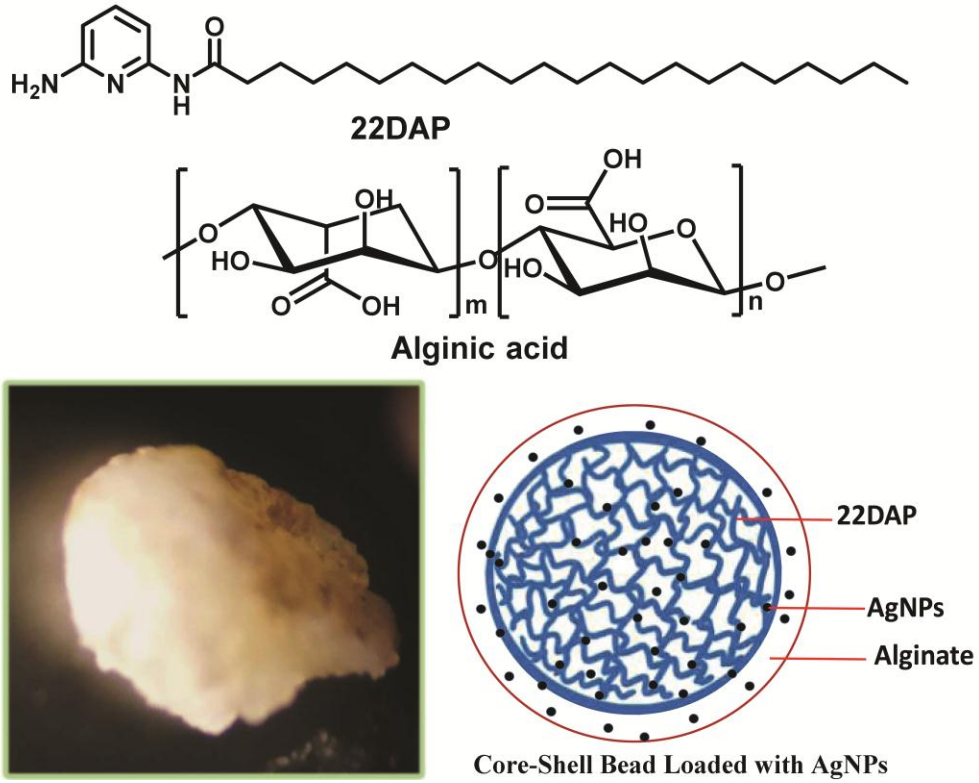


Figure 2. Structures of **22DAP** and alginic acid, microscopic image (left) of hybrid **22DAP**/alginate gel bead loaded with AgNPs and graphic diagram (right) of an AgNPs-loaded core–shell gel bead.

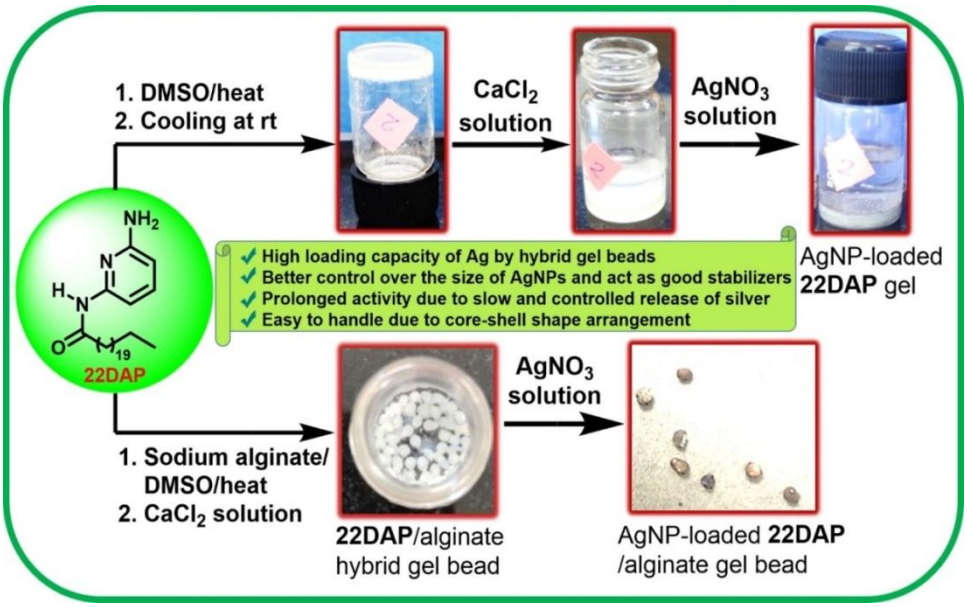


Figure 3. *In situ* preparation of silver nanocomposite **22DAP** gel and **22DAP**/alginate hybrid gel beads.

In addition, comparative study for silver uptake and release was carried out in a single component **22DAP** gel, extended **22DAP**/alginate hybrid gel and gel beads. Notably, the previous reports based on hybrid gel beads showed less uptake of AgNPs (3 – 4 equivalents of gelator). Therefore, the **22DAP**/alginate hybrid gel beads were prepared which showed better efficiency of silver uptake (~10 equivalents) due to the large surface area. Furthermore it has also shown excellent control on the size of AgNPs and slow release of AgNPs making it an ideal antimicrobial formulation which ensures prolonged release of drug. It is evident that the bead shape of these nanocomposites will make it easier to handle for use in wound repair, biosensors, bone healing and surgical interventions.

Chapter 4: Aminopyridinyl Tricosanamide Based Pseudoplastic and Thermoreversible Oleogels for pH-Dependant *in vitro* Release of Metronidazole

This chapter provides a brief outline about the importance of oleogels. The preparation of oleogels have attracted the attention of researchers due to their wide applications in the fields of pharmaceuticals, cosmetics and food industries. Therefore, in this chapter, we have designed a new oleogel formulation for topical and transdermal applications of metronidazole (antimicrobial and antiseptic agent) with enhanced properties (**Figure 4**).

Aminopyridinyl tricosanamide fatty acid amide oleogelator self-assembled in edible oils, form stable and thermoreversible gel with good shear thinning and pseudoplasticity. These oleogels may be ideal drug delivery vehicles for topical and transdermal applications due to their shear thinning and pseudoplastic behaviour. In addition, the pH of these gels which is in the range of pH of the skin, makes it more attractive as it would prevent irritation during application. Furthermore, these gels show

a slow and controlled release of the drug in both acidic and slightly basic buffers, demonstrating the effectiveness of these gel formulations which ensure long-term activity. These results can present good opportunity in the field of cosmetics, foods and pharmaceuticals.

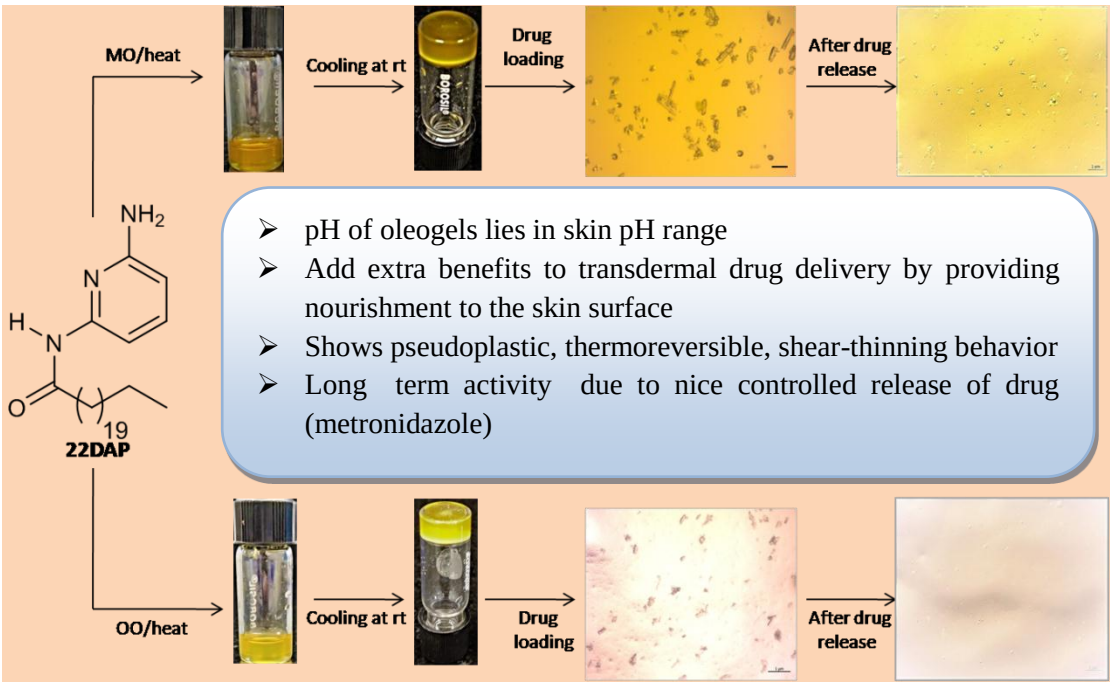


Figure 4. Preparation of MOG (mustard oil gel) and microscopic images of drug (metronidazole) encapsulated MOG before and after drug release (above); and preparation of OOG (olive oil gel) and microscopic images of drug encapsulated OOG before and after drug release (below).

Chapter 5: Towards the Synthesis of Glycodendrimers for Drug Delivery Applications

This chapter delivers a brief plan about the importance of dendrimers. The synthesis of denrimers is of great interest because of their tree-like embranchment that are nano-sized, highly functional three dimensional symmetric molecules with well-defined, monodisperse, and homogenous composition which make them as ideal candidates for

use in nanotechnology and a variety of biological applications. This chapter describes the synthesis towards glycodendrimers for drug delivery applications.

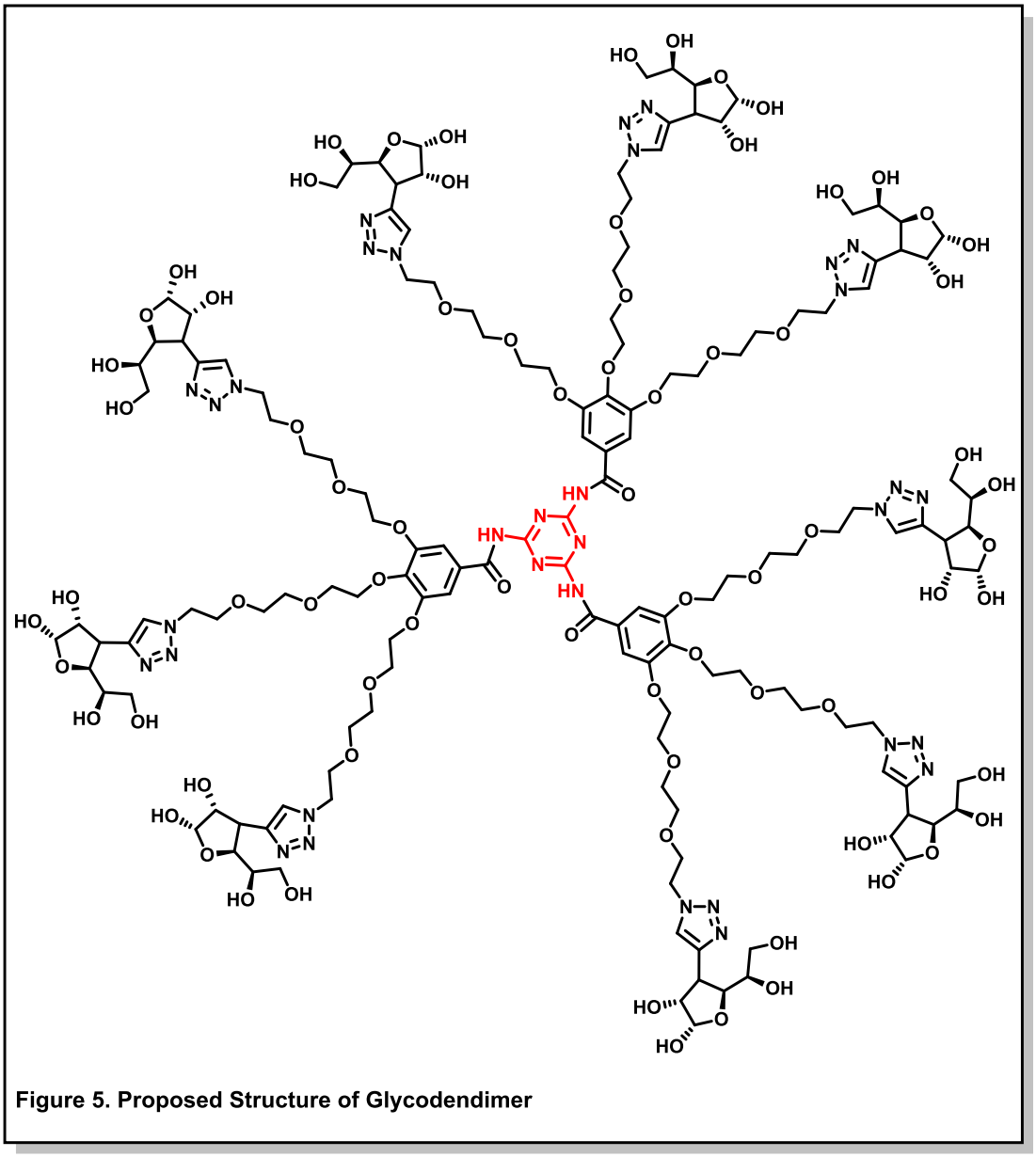


Figure 5. Proposed Structure of Glycodendimer

Therefore, we proposed to synthesize glycodendrimer (**Figure 5**) using melamine as a core. Here we have chosen melamine as a core for synthesis of glycodendrimers because it is commercially available, highly stable even at exposure of high temperature, flame retardant, moisture resistance and hence can enhance bioavailability

of drugs. The synthetic efforts were made to construct the proposed glycodendrimer, but unfortunately we could not achieve the target even after many efforts. It therefore needs to be further optimized before proceeding to achieve the proposed glycodendrimer synthesis. The effort in this direction are presently being perused in our laboratory.