solution gets displaced. Concerta® (Methylphenidate HCl), Teczem® (Enalapril Diltiazem), Acu System C® (Vitamin C), Osmosin® (Indomethacin), and Volmax® (Albuterol) are examples of marketed preparations that use the OROS technology [67].

Alza Corporation also developed a liquid osmotic system (L-OROS) for delivering liquids, solid dispersions, or liquid–liquid emulsions [68, 69]. L-OROS is a capsule-based osmotic system. It comprises a drug layer that is in liquid form, an osmotic push layer, and a coating of a semipermeable membrane. When the system comes in contact with water, it permeates the membrane, reaches the osmotic layer, and activates it, which causes an expansion of the osmotic layer, thus forcing out the liquid formulation [67].

LEK Pharmaceuticals obtained a patent for controlled-release tamsulosin hydrochloride tablets in 2007. The tablets were based on an oral controlled absorption system (OCAS) that consists of a matrix of gel-forming and gel-enhancing agents, which helps in a constant release of the drug, unaffected by the presence of food or fluid. It was clinically proven that the OCAS system reduced the drug peaks and attained continuous drug release. Furthermore, it results in reduced adverse effects [70].

Penwest Pharmaceuticals filed a patent for TIMERx technology in 1995. This technology enabled to achieve a zero-order or first-order drug release and provide a flexible platform for drug delivery—chronotherapeutic drug delivery—by shifting from a mere "factory-fixed" system to a physicochemical controlled system. TIMERx is composed of two heterodisperse polysaccharides that are obtained naturally. The two polysaccharides self-assemble to form a complex 3D structure. The interactions that occur between the two polymers are engineered to entwine, disentangle, entangle, or dissolve them in time in response to physiological conditions or according to requirements. Cystrin CR® (oxybutynin) was the first marketed product that used TIMERx technology. Since then, many products have been marketed using TIMERx such as Slofedipine XL® (nifedipine) and Cronodipin® (nifedipine). Procardia XL® was developed to attain zero-order drug release, in collaboration with Mylan that received the FDA's approval [71].

Elan has developed technologies to satisfy the need of the drugs, including spheroidal oral drug absorption system (SODAS), intestinal protective drug absorption system (IPDAS), and chronotherapeutic oral drug absorption system (CODAS). SODAS is a multilayered tablet that produces controlled release beads. This technology provides flexibility, that is essential for customized dosage forms that satisfy individual needs (in the case of blood pressure management or pain). It leads to a pulsatile drug release. Ritalin LA and Focalin XR are examples of formulations using this technology to treat attention-deficit hyperactivity disorder. Once-daily dose is sufficient to acquire a pulsed profile that offers efficacy throughout the day [72].

IPDAS is a system that is used for GI irritant drugs, including nonsteroidal antiinflammatory drugs. It is composed of many controlled-release, high-density beads that are compressed into a tablet. After its ingestion, it disintegrates and disperses the beads, thus releasing the drug in the stomach. It then passes along the GIT in a gradual and controlled manner. The drug release depends on the polymer used for bead coating. Naprelan® (Naproxen) uses IPDAS technology. It is well tolerated and has an onset of pain relief within 30 min that lasts for a day.

CODAS was developed for the drugs whose immediate release is undesirable. Here, the drug release is programed to take place after a prolonged interval, following administration. Verelan PM® (Verapamil) for bedtime dosing uses CODAS technology. It consists of pellet-filled capsules. The delay is because of applying a nonenteric polymer (water-soluble or water-insoluble polymer combination) to the drug-loaded pellets. When the water comes in contact with a water-soluble polymer, the water-soluble polymer dissolves and results in drug release. The water-insoluble polymer remains as a barrier, thus maintaining a controlled release. It was successful in attaining a delay in drug delivery for 4–5 h [73].

10. FUTURE PERSPECTIVE

The amount of novel molecules entering the market has decreased in the past 10 years. However, the funding for the pharmaceutical research and development has doubled in the last 20 years. As a result of this, the advent of novel drug delivery systems has grown remarkably to a point today, where we have so many different formulations to choose from [74]. These advanced controlled delivery systems have enormous potential to improve the therapeutic efficacy. Combination of various approaches will enable us to achieve a better therapeutic response [75].

Also, because they are administered by oral route, they improve the patient's compliance. The new therapeutics under development are for the macromolecules such as proteins, peptides, and vaccines. Oral controlled-release formulations of these macromolecules will be very beneficial. The development of the current formulations for increasing efficiency and reducing cost is also important.