TABLE 2
List of various hydrophilic and hydrophobic polymers reported for their application in controlled-release solid oral products.

Hydrophilic polymers	Hydrophobic polymers
Hydroxypropylmethyl cellulose (HPMC)	Ethyl cellulose
Hydroxypropyl cellulose (HPC)	Cellulose acetate
Hydroxyethyl cellulose (HEC)	Cellulose acetate phthalate
Sodium carboxymethyl cellulose (Na-CMC)	Polymethacrylates
Sodium Alginate	Polyvinyl acetate
Xanthan gum	Polyvinyl chloride
Chitosan	Polypropylene

4.1. Hydrophilic Polymers

Hydrophilic polymers are primarily employed in the preparation of matrix or monolithic system. Hydrophilic matrix systems are the most frequently used systems for design of oral-controlled drug delivery as they are easy to handle, reproduce a desirable drug profile, and are cost-effective. When a matrix tablet is wetted by the GI fluids, the surface forms a gel layer, whereas the core is unaffected. Slowly, as more and more water penetrates into the tablet, the thickness of the gel layer increases and drug diffuses out through the gel layer. Also, as the hydration increases, the surface polymer starts eroding from the matrix surface. Soluble drugs are released initially with diffusion control and at a later stage with the combination of diffusion and polymer erosion, whereas insoluble drugs are predominantly released by erosion [29].

Regulatory agencies have approved a number of hydrophilic polymers for oral formulations, namely cellulosic polymers such as methylcellulose, hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose, hydroxyethyl cellulose, and sodium carboxymethylcellulose (NaCMC); noncellulosic polymers such as Sodium alginate, Xanthan gum, Gum agar; and other polymers such as Carbomers. Few of the most widely used hydrophilic polymers are discussed herewith [30–32].

4.1.1. Hydroxypropyl methylcellulose

HPMC is a mixture of alkyl hydroxyalkyl cellulose ether containing methoxyl and hydroxypropyl groups. It offers a range of advantages, such as rate-controlling polymer in terms of stability, nonionic nature, direct compression compatibility, and pH-independent release. It is stable in a wide range of pH 3–11 [33] and resistant to enzymatic degradation [32]. HPMC is available in different grades identified by the alphabetical letter "A, E, F, and K" based on the different proportions of hydroxypropoxyl and methoxyl substitutions. The relative proportion of these two substituents influences the drug release as the hydrophilic nature of the hydroxypropoxyl group, and the hydrophobic nature of the methoxyl group determines the motility of water in the gel layer. Nokhodchi found that out of a large number of grades available, the best ones for sustained release formulations are K4M and K100M because of their high tensile strength [34], where 4M and 100M refer to the viscosity of 2% aqueous solution of HPMC (4000 cps and 100,000 cps, respectively).

4.1.2. Sodium carboxymethylcellulose

NaCMC is a hydrophilic, anionic semisynthetic polymer available in different viscosity grades with different degrees of substitution similar to HPMC. NaCMC is highly pH sensitive and shows different characteristics in a different environment. The aqueous solution of NaCMC is stable in the pH range of 4–10 but precipitates below pH 2 and loses viscosity above pH 10 [32]. Formulations containing NaCMC as rate-controlling polymer shows release primarily by erosion mechanism, but at pH 1.0, the gel layer solidifies, resulting in a release through diffusion mechanism [35]. A number of studies found that the release rate can be controlled even better, using a mixture of HPMC and NaCMC [36]. The polymer tends to form a complex with the drug further slowing the release [37,38].

4.1.3. Sodium alginate

Sodium alginate is a naturally derived polysaccharide polymer obtained from marine brown algae. Chemically, it is composed of two building blocks, namely α-D-mannuronic acid (M-Block) and β-L-guluronic acid (G-Block) units [39]. The length of the unbranched sequential distribution of M and G blocks varies depending on the source from which the polymer is obtained. Similar to NaCMC, sodium alginate is pH sensitive as well. The pH sensitivity of alginates can be attributed to carboxylate groups that can both accept and release protons. It was revealed from cryogenic electron microscopy that the hydrated surface of sodium alginate matrix tablets in the simulated gastric fluid was particulate and porous as when compared with the continuous gel layer in simulated intestinal fluid [40]. Hence, sodium alginate shows pH-dependent drug release. Even after such flexible