

*Review Article*

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**Functional Polymers: A Review****Sachin Mane***Polymer Science and Engineering Division, National Chemical Laboratory, Pune – 411008, India.**Department of Chemistry, Indian Institute of Technology, Bombay, Mumbai – 400076, India.**\*Corresponding Author, Email: stm2011.mane@gmail.com***Received:** April 24, 2016**Revised:** July 12, 2016**Accepted:** July 16, 2016**Published:** July 26, 2016

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**Abstract:** The present review is interested in discussing the effect of polymerization, functionalization, and physicochemical parameters on reactivity of functional polymer microbeads (FPMBs). FPMBs have the small reactivity since most of the functional groups are well-buried into the matrix. FPMBs with greater reactivity can be obtained by considering two main approaches. In first approach, effect of polymerization (suspension, emulsion, or dispersion) and functionalization (direct-, post-polymer functionalization, or functional group transformation) on FPMBs are discussed. In second approach, effects of physico-chemical parameters on reactivity of FPMBs are explained. Effect of different parameters on polymer properties such as surface area, pore volume, pore size, thermal properties, and morphology are also discussed. Moreover, applications of functional polymers in solid-phase synthesis, solid-phase extraction, and biomedical fields are elaborated.

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**Keywords:** Functional polymeric microbeads; Functionalization methods; Polymer applications; Suspension polymerization

**1. INTRODUCTION**

Over the last decade, designing of functional polymeric microbeads (FPMBs) have been paid an increased commercial attention due to their potential applications [1–3]. The polymer properties such as reactivity, surface area, pore volume, pore size, porosity, rigidity, stiffness, thermal degradation, and glass transition temperature are highly tunable and controllable. In suspension polymerization, physico-chemical parameters significantly affect the aforementioned properties [4]. These properties can be improved upto a certain extent and above this it is not possible to improve these properties. For instance, thermal degradation and glass transition temperature can be increased by varying monomer, cross-linker, and their feed composition [5,6]. Further, surface area, pore volume, and pore size are tunable upto a certain limit by varying porogen and their concentration [7]. These limitations are due to the organic composition of FPMBs and method of polymerization. Therefore, studying the influencing parameters for improving the reactivity of FPMBs is very important. FPMBs with desired functionality and properties significantly increase the polymer efficiency.

Parameters such as method of polymerization, functionalization, cross-link density, porogen, and stirring speed of a reaction composition influence the reactivity of FPMBs. In these parameters, type of polymerization, functionalization, and cross-link density are the major (primary) parameters whereas porogen and stirring speed are the minor (secondary) parameters that affect reactivity of FPMBs. FPMBs

obtained by a suspension polymerization have the greater rigidity and stiffness compared to emulsion or other polymerization techniques [8–10]. Engstrom *et al.* [11] showed that FPMBs can promisingly act as a support material in solid-phase synthesis. The FPMBs have the potential applications in different fields [12–17] which underlines the importance of the present review.

This review is interested in designing of reactive FPMBs by a free-radical suspension polymerization. The role of major (primary) and minor (secondary) influencing parameters in obtaining FPMBs are discussed in details. This review provides the pathway for obtaining the desired FPMBs by direct-, post-functionalization, and functional group transformation. In addition to this, most important properties and applications of FPMBs are also discussed.

## 2. FUNCTIONALIZATION

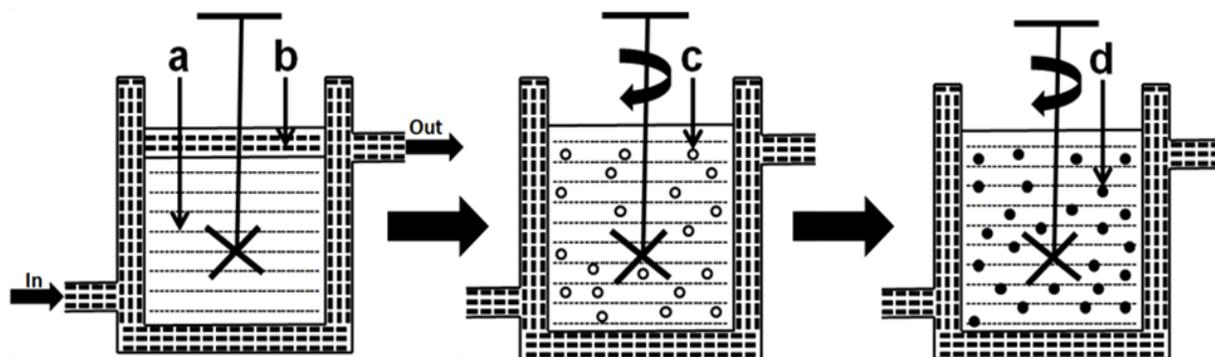
Over the past few years, FPMBs have an increased attention due to their interesting properties and potential applications in various fields [18,19]. FPMBs are unique materials which are extensively used in solid-phase synthesis, solid-phase extraction, and biomedical applications [20–22]. In addition to polymer functionality, other properties such as surface area, pore volume, pore size, and hydrophilicity-hydrophobicity of FPMBs are also an important [23]. Polymer functionalization is classified depending on the method of functional polymer synthesis [24] which consists of three main types, direct-functional polymer synthesis (*in-situ*), post-functionalization (post-polymer modification), and functional group transformation. These functionalization methods are discussed below.

### 2.1. Direct (*in-situ*) functionalization

Functional vinyl monomer containing pendant ester, hydroxyl, epoxy, amine, carboxylic acid, thiol, ketone, or aldehyde can be polymerized directly by free-radical polymerization to obtain FPMBs in the absence [25] or in the presence of a cross-linker [26] called as direct functional polymer synthesis. In suspension polymerization, functional vinyl monomer can be polymerized by direct free-radical polymerization. The polymerization of methyl methacrylate, acrylic acid, methacrylic acid, or 2-hydroxyethyl methylacrylate with hydrophilic cross-linker (ethylene dimethacrylate/trimethylolpropane triacrylate/pentaerythritol triacrylate/tetraacrylate) or hydrophobic cross-linker (divinylbenzene) can be carried out depending on the desired properties of FPMBs. In the past, Ohtsuka *et al.* [27] reported the direct functionalization of carboxylic acid, sodium sulfonate, pyridine, and dimethyl amine based polymer which was obtained using ethylene dimethacrylate as a cross-linker by a suspension polymerization. Monomer and cross-linker can be varied according to the desired functionality and hydrophilic/hydrophobic properties of FPMBs. Most common monomers and cross-linkers used for direct free-radical suspension polymerization are reported in the literature [5]. The schematic representation of a suspension polymerization [28] to obtain FPMBs by direct polymerization is represented in **Figure 1**.

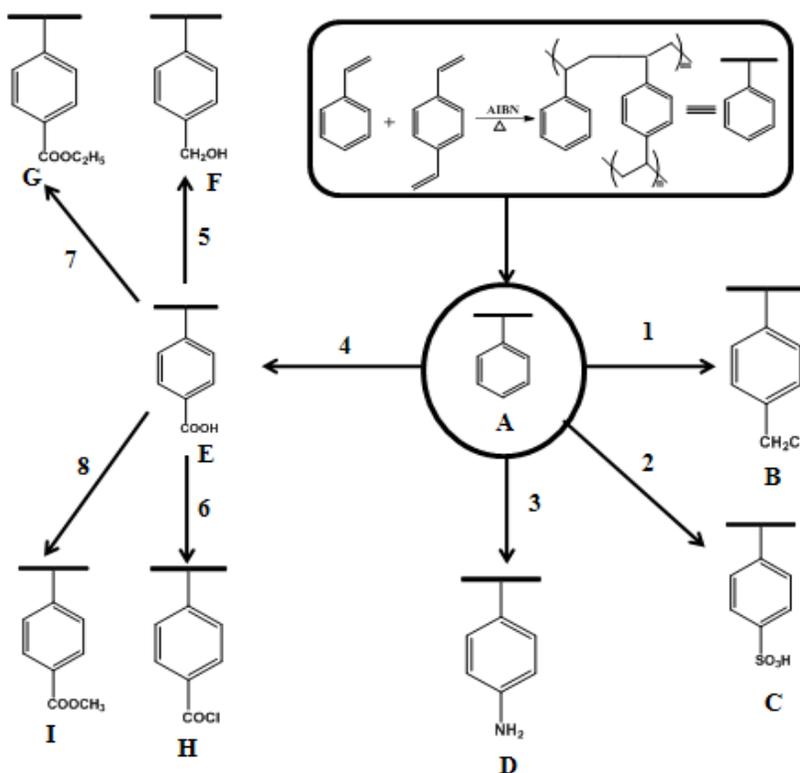
### 2.2. Post-functionalization (*post-polymer modification*)

In some of the cases, obtaining of desired FPMBs by direct-polymerization is not possible because certain functionality may interfere during polymerization [29]. In this case, post-functionalization is preferable and widely used method. The post-functionalization is a very old technique and some of the examples are provided herein. In 1847, Oesper *et al.* [30] converted the cellulose into a nitrocellulose by direct exposing cellulose to nitric acid. In the early 1960s, Iwakura *et al.* [31] used the pendant epoxy functionality for the post-modification. In post-functionalization, synthesis of the non-functional polymer, for instance, poly(styrene-*co*-divinylbenzene) and subsequent modification to obtain FPMBs can be



**In and Out:** hot water circulation, **a:** aqueous phase, **b:** organic phase, **c:** spherical FPMBs before polymerization (before heating), **d:** formation of FPMBs after polymerization (after heating).

**Figure 1.** Schematic representation of suspension polymerization.



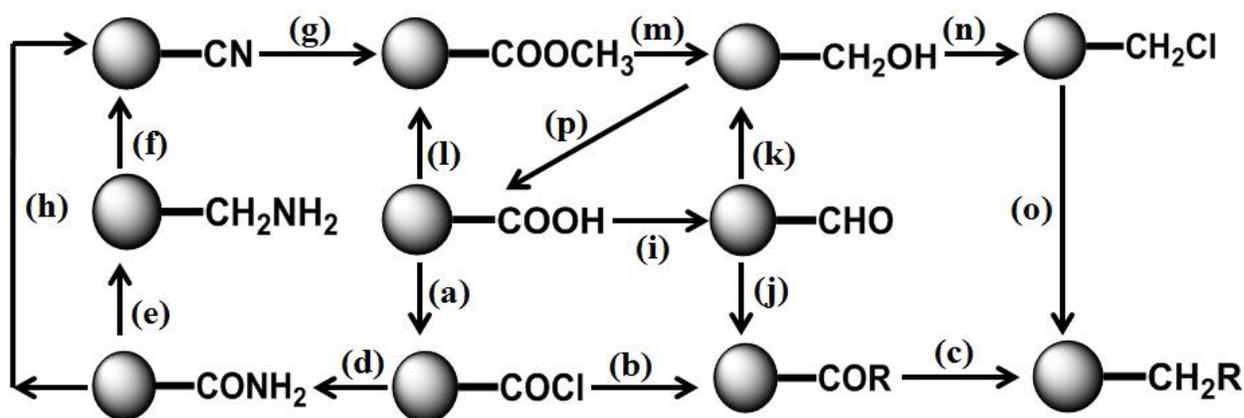
(1) Blanc chloromethylation,  $\text{ZnCl}_2$ ,  $\text{HCl}$ ,  $\text{CH}_2\text{O}$ ; (2) sulphonation, conc.  $\text{H}_2\text{SO}_4$ , heat for 7–8 h; (3) amination,  $\text{HNO}_3 + \text{H}_2\text{SO}_4$  followed by  $\text{SnCl}_2/\text{HCl}$ ; (4) carboxylation,  $[(\text{IPr})\text{AuOH}]$ ,  $\text{CO}_2$ ,  $\text{KOH}$ ,  $\text{THF}$ ,  $20^\circ\text{C}$ , 12 h followed by aq.  $\text{HCl}$  [36]; (5) reduction,  $\text{LiAlH}_4$ ,  $\text{H}_3\text{O}^+$ ; (6)  $\text{SOCl}_2$ ; (7) esterification,  $\text{H}_2\text{SO}_4$ ,  $\text{CH}_3\text{OH}$ ,  $64^\circ\text{C}$ ; (8) esterification,  $\text{H}_2\text{SO}_4$ ,  $\text{EtOH}$ ,  $78^\circ\text{C}$ .

**Figure 2.** Synthesis of FPMBs by post-functionalization.

carried out [32]. In the 1950s, chlorinated poly(styrene-*co*-divinylbenzene) beads were used as an ion exchange resin [33]. Over the last decade, poly(styrene-*co*-divinylbenzene) is most widely used copolymer for post modification. Serniuk *et al.* [34] used thiol-ene addition (click) reaction for butadiene functionalization. Recently, number of post-polymer modification methods such as thiol-ene addition, epoxides, anhydrides, oxazolines, isocyanates, active esters, thiol-disulfide exchange, Diels-alder reactions, Michael-type addition, and azide-alkyne cycloaddition reactions are available. By this method, a polymer containing aldehyde, ester, ketone, and hydroxyl functionality can be obtained which are previously reported in the literature [35]. By post-polymerization method, thiolation, sulphonylation, chloromethylation, carboxylation, formylation, esterification, alkylation, acylation, or amine functionality can be inserted into the polymer to obtain desired functional beaded polymer. Different methods of post-functionalization of non-functional polymer are represented in **Figure 2**.

### 2.3. Functional group transformation

This type of functionalization method is mostly used when a particular functional polymer is difficult to obtain by direct polymerization and post-functionalization [29]. In this method, synthesis of the non-desired functional polymer by a direct or post-functionalization and subsequent modification into desired functional polymer using functional group transformation such as oxidation or reduction are carried out [37,38]. In 2008, Jacob *et al.* [39] modified the ester monomer functionality into a hydroxyl group which was then reacted with an epoxy compound to obtain hydroxyl functionalized cross-linker. This cross-linker was then polymerized with styrene to obtain a cross-linked hydroxyl polymer. Apart from this, polymer reactivity can be improved by a core-shell approach as mentioned in the literature [40]. The functional group of poly(acrylic acid-*co*-divinylbenzene) can be converted into different functional groups by a functional group transformation as shown in **Figure 3**.



(a):  $\text{PCl}_5$  or  $\text{SOCl}_2$  in pyridine; (b):  $\text{R}_2\text{CuLi}/\text{Et}_2\text{O}/-78^\circ\text{C}$  or  $\text{R}_2\text{Zn}/\text{FeCl}_3/\text{THF}/-10^\circ\text{C}$  [41]; (c): MeOH,  $\text{NaBH}_4$ , reflux; (d):  $\text{NH}_3$  in pyridine; (e): MeOH,  $\text{NaBH}_4$ ; (f): 2 eq. DMP (Dess-Martin pyridinane)  $\text{CH}_2\text{Cl}_2$ ,  $25^\circ\text{C}$ , 10–15 min [42]; (g):  $\text{TMSCl}$ , 2 MeOH,  $\text{H}_2\text{O}$  [43]; (h)  $\text{PhSiH}_3$  (1 eq.), TBAF ( $\text{Bu}_4\text{NF}_5$ ), toluene,  $100^\circ\text{C}$ , 1–3 h [44]; (i):  $\text{SOCl}_2$  in pyridine,  $\text{pd}(\text{dba})_2$ ,  $\text{PMeS}_3$ ,  $\text{Et}_3\text{SiH}$  or  $\text{Ph}_2\text{MeSiH}$ , toluene,  $40^\circ\text{C}$ , 3 h [45]; (j): (i) 1,3-dithiane,  $\text{H}_3\text{O}^+$  (ii)  $n\text{-BuLi}$ , THF,  $\text{R-X}$  (X: halogen) (iii)  $\text{HgO}$ ,  $\text{H}_2\text{O}/\text{THF}$  [46]; (k): MeOH,  $\text{NaBH}_4$ , reflux; (l): esterification,  $\text{CH}_3\text{OH}$ ,  $\text{H}_2\text{SO}_4$ , reflux; (m): THF,  $\text{LiAlH}_4$  followed by ethyl acetate; (n):  $\text{ZnCl}_2$ ,  $\text{HCl}$  or  $\text{SOCl}_2$ , pyridine; (o):  $\text{RLi}$ , or  $\text{R-Mg-Cl}$ , or  $\text{R}_2\text{Zn}$ , or  $\text{R}_2\text{CuLi}$  [47]; and (p): oxidation,  $\text{KMnO}_4/\text{H}_2\text{SO}_4/100^\circ\text{C}$ , or  $\text{K}_2\text{Cr}_2\text{O}_7/\text{H}_2\text{SO}_4/100^\circ\text{C}$ . [ $\text{R}$  = alkyl, or aryl].

**Figure 3.** Synthesis of FPMBs by functional group transformation.

### 3. FPMBs REACTIVITY AFFECTING PARAMETERS

Major (primary) parameters that affects to FPMBs reactivity are type of polymerization (condensation or free-radical polymerization), functionalization methods, and cross-link density (monomer-non-functional cross-linker feed composition). The condensation polymerization method can be used to obtain the functional polymer in the form of powder that has the greater surface area than other polymerization techniques. In free-radical polymerization, suspension, emulsion, or dispersion methods have their own characteristics and offers functional polymers in the form of microbeads, emulsion, or powder. FPMBs obtained by a suspension polymerization have the greater strength, rigidity, and stiffness with tunable surface area, pore volume, and pore size [48]. Due to these properties, FPMBs obtained using suspension polymerization has significant importance than functional polymer obtained by other polymerization techniques. Further, functionalization (direct, post-functionalization, and functional group transformation) methods as mentioned above are also the important parameter. If the functionalization is carried out using a functional monomer and a non-functional cross-linker, then lower cross-link density (non-functional cross-linker) polymer offers greater FPMBs reactivity [28,49]. This is due to the concentration of functional monomer decreases as cross-link density increases (non-functional cross-linker).

The porogen and stirring speed of a reaction mixture are the minor (secondary) parameters that also affect the reactivity of FPMBs. The suspension polymerization is widely used for free-radical polymerization where the reaction compositions are functional monomer (one double and functional group) and functional or non-functional cross-linker (with at least two double bonds). A porogen affects the surface area and porous (pore volume, pore size, and porosity) properties which attributes to the FPMBs reactivity [50,51]. Even at same cross-link density of a polymer, different porogens have the different characteristics to generate surface area and porous properties resulting into different polymer reactivity. The solvating porogens have the property to generate greater surface area and microporosity (small pore volume and pore size) compared to non-solvating porogen at the same cross-link density [52,53]. The high surface area increases functional group availability on the surface [49]. Thus, solvating porogen enhances the surface area for functional group availability than non-solvating porogen. In minor (secondary) parameter, stirring speed is also one of the reactivity affecting parameters. The high and slow stirring speed generates smaller and larger particle size of FPMBs, respectively [54] because stirring speed ( $d$ ) and average particle size ( $N$ ) are inversely proportional to one another [Equation 1]. The functional group content per gram of polymer is higher for smaller particle size and vice-versa for larger particle size of FPMBs. This is due to most of the functional groups of larger particle size are well-buried into the polymer matrix which are not available for the application [55].

$$d = k \frac{D_v \cdot R \cdot V_o \cdot \epsilon}{D_s \cdot N \cdot V_a \cdot C_p} \quad (1)$$

where,  $d$  is the average particle size,  $k$  is the parameter of reactor dimension,  $D_v$  is the reactor diameter,  $D_s$  is the stirrer diameter,  $R$  is the volume ratio of the organic to the aqueous phase,  $N$  is the stirring speed,  $v_o$  and  $v_a$  are the viscosity of the organic and aqueous phase, respectively,  $\epsilon$  is the interfacial tension of the two (aqueous and organic) phases, and  $C_p$  is the concentration of a protective colloid.

#### 4. FUNCTIONAL POLYMER CHARACTERIZATION

The characterization of FPMBs before and after modification is an important to obtain more efficient polymer. An evaluation of surface area, pore volume, pore size, porosity, thermal (thermal degradation/glass transition temperature), and morphological properties are important before use of FPMBs in different fields. These properties are discussed below.

##### 4.1. Surface area

Surface area is a key parameter for obtaining more efficient polymer. The physico-chemical parameters including porogen type, porogen amount, reaction time and temperature, stirring speed, and concentration of a protective colloid affect the polymer efficiency. Indeed, porogen type and their amount are most influencing parameter which affects the surface area. Solvating porogens have the tendency to generate greater surface area polymer compared to non-solvating porogen. On the other hand, higher amount of solvating porogens increases the surface area. However, increase or decreases of these porogens is allowed upto a certain extent. After certain amount of porogen, emulsion formation takes place which do not allow the bead formation. Therefore, balancing the amount of a porogen in monomer composition is an essential.

##### 4.2. Pore volume and pore size

Depending on the composition, porous materials are classified into three main types, organic polymeric material, inorganic nanoparticles, and organic-inorganic hybrid (metal-organic framework). Moreover, depending on pore size, porous materials are classified into micro, meso, and macroporous [56]. The same factors mentioned in surface area are also attributes for variation in pore volume and pore size. Indeed, solvating and non-solvating porogen generates micro/meso and meso/macro porous polymeric beads, respectively. A porogen is the most influencing parameter to the porous properties whereas other parameters affects in a small extent. The effect of type and amount of a cross-linker on surface area and porous properties is discussed in the published literature [51].

##### 4.3. Thermal study (thermal degradation/glass transition temperature)

Thermal properties such as thermal degradation/glass transition temperature of FPMBs are also an important and considered during application as a solid-support in high temperature solid-phase synthesis. Different parameters such as rigidity, flexibility, and amount of a monomer and crosslinker affect the thermal behaviour of FPMBs. Our recent study reported that, high rigidity in monomer/crosslinker and their greater amount in polymer composition increases the thermal degradation and glass transition temperature. Opposite results were observed for the flexible monomer, crosslinker, and their higher amount in polymer composition. We have reported, these variations in thermal properties with respect to type and amount of a monomer and crosslinker [28,49].

##### 4.4. Morphology

External morphology of polymeric beads affects their efficiency. In general, conglomerated property decreases inversely non-conglomerated property increases the efficiency of FPMBs in solid phase synthesis. Our recent publication showed that, hydrophilic polymeric microbeads have the property of conglomeration whereas hydrophobicity decreases the conglomeration [28,49]. Morphological properties of polymeric beads can be controlled by balancing the type of a monomer, crosslinker, and their feed composition. Effect of porogen on morphology of polymeric microbeads are published in the

literature [28,49,51].

## 5. FUNCTIONAL POLYMER APPLICATIONS

Different types of functional materials such as organic porous polymer, inorganic nanoparticle, and metal-organic framework have their own merits and demerits. Porous functional polymers were potentially used due to their inexpensive, ease of preparation, and recyclability. Nowadays, FPMBs have an increased commercial attention due to their interesting properties such as surface area, pore volume, pore size, porosity, hydrophilic-hydrophobic balance, thermostability, and morphology. FPMBs have several advantages over other functional materials and have potential applications in solid-phase synthesis/extraction and biomedical field as mentioned below.

### 5.1. Solid-phase synthesis

The application of FPMBs in solid-phase synthesis is very old and still attractive due to ease of recyclability. Different immobilization methods such as adsorption, covalent confinement, ionic, and entrapment can be used for the immobilization of a catalyst, reagent, substrate, photosensitizer, scavenger, or protecting groups. From the application point of view, solid-phase synthesis has the advantages as well as disadvantages. Some attractive features of crosslinked polymer in solid-phase synthesis are simplification in work up, ease of isolation, and regeneration of the functional polymers. The crosslinked polymeric support should be insoluble in common solvents, inert toward catalysts, reagents, substrate, and reaction medium, capable for high degree of functionalization, must have high degree of swelling capacity, and physico-chemically compatible with supported entities. A solid-support can be easily separated from low molecular weight compounds by a simple filtration. In case of soluble functional polymers, ultra-filtration or selective precipitation is needed for polymer recovery. Along with attractive features, polymeric supports have some disadvantages such as time consuming solid-support synthesis, small reactivity, slow reaction rate, less yield, and reaction conditions should be mild and non-destructive to the polymer. These disadvantages can be overcome by proper selection of a solid-support. The published literature reported the importance of hydrophilic polymer in solid-phase synthesis. Engstrom *et al.* [11] describes the importance of hydroxyl functionalized hydrophilic polymer beads as a solid-support in solid-phase synthesis. Further, Kita *et al.* [57] reported the application of hydrophilic poly(ethylene glycol) methacrylate beads in solid-phase synthesis of hydantoins.

### 5.2. Solid-phase extraction

The use of FPMBs in solid-phase extraction is also one of the most important fields. Most inexpensive adsorbing agent is activated carbon and is tremendously used for extraction process [58]. However, non-selective adsorbing agent decreases the adsorbent efficiency. Different selective extracting agents such as polymer-supported calixarene, crown ether, and cryptands are widely used in a selective extraction process. The properties of functional polymer used for immobilization of chelating or extracting agents can be controlled by varying physico-chemical parameters. Vasapollo *et al.* [59] discussed the applications of molecularly imprinted polymers in solid-phase extraction. Javanbakht *et al.* [60] studied the extraction of important drug molecules from biological samples such as plasma and urine. Functional polymers are tremendously useful in extraction of hazardous/toxic metals and anionic/cationic dyes. In addition to this, polymers are also useful in extraction of different food matrix analytes such as simazin, propazine, and propazine methacrylate. Further, extraction of several compounds in different sample matrices such as biological, environmental, and food sample can be carried out. Sellergren *et al.*

[61] used the molecular imprinted polymers for extraction of pentamidine drug which is useful in treatment of AIDS related disease. Caffeine and theophylline are drug molecules especially useful for central nervous system (CNS) stimulant and in therapy of respiratory diseases, respectively. In addition, they have some disadvantages and side effects also. Tian *et al.* [62] were synthesized an ionic liquid modified polymer for the extraction of caffeine and theophylline from green tea. Ergot alkaloids such as ergometrine, ergosine, ergotamine, ergocristine, ergocryptine, and ergocornin are essential for human being. However, their excess intake in human body can cause nausea, convulsions, hallucinations, and vasoconstriction which lead toward gangrenous symptoms and abortion. This toxicity is due to interactions with  $\alpha$ -adrenergic, serotonergic, and dopaminergic receptors. Therefore, extraction of excess of ergot alkaloids is an essential. Lenain *et al.* [63] developed the molecular imprinted polymer beads for the extraction of ergot alkaloids. Agrochemicals such as fungicide, pesticide, and herbicide are most attributing for environmental pollution especially for water contamination. Therefore, extraction of these agrochemicals is an important. In 2013, Yi *et al.* [64] discussed the applications of molecular imprinted polymers in extraction of agrochemicals. Organochlorine pesticides (OCPs) are also a toxic agrochemical and have adverse effect to human and animals. In some of the countries, their use is banned. However, OCPs are being used in several countries for agriculture and public purpose. Gulbakan *et al.* [65] were obtained poly(styrene-divinylbenzene) microbeads for the extraction of OCPs.

### 5.3. Biomedical applications

The biomedical engineering is one of the fastest growing research areas and still relatively less developed. Chitosan polymer is most widely used for biomedical applications due to its biocompatible, biodegradable, nontoxic, hypocholesterolemic, immunoadjuvant, antiviral hypolipidemic, mucoadhesive, haemostatic, antimicrobial, and antitumoral properties [66]. Moreover, poly(methyl methacrylate) is used in applications such as bone cements, rigid intraocular and contact lenses, and dental fillings [67]. FPMBs have potential applications such as fillers and bulking agents, embolic particles, and drug delivery vehicles [68]. Ahmed *et al.* [69] mentioned the various applications of polymeric hydrogels in drug delivery, pharmaceuticals, tissue engineering, diagnostics, wound dressing, separation of biomolecules or cells, regenerative medicines, and biomedical fields. Leong *et al.* [70] discussed the polymeric applications in cell culture and cell delivery. They concluded that, polymeric microspheres are inexpensive and more efficient having applications in cell expansion, biomolecule harvesting, cell therapeutics, and tissue engineering.

## 6. CONCLUSIONS

In conclusion, desired FPMBs with greater reactivity can be obtained using a suitable polymerization and functionalization method, as well as by controlling physicochemical parameters. The major (primary) affecting factors are method of polymerization, functionalization, and cross-link density whereas minor (secondary) parameters are porogen and stirring speed that significantly affects the reactivity of FPMBs. The polymer containing desired functional group can be obtained by a direct-polymerization (*in-situ*), post-polymer functionalization, or functional group transformation. These functionalization methods offer different way of insertion of functionality into the polymer microbeads. In addition to this, physico-chemical parameters also affect the reactivity, surface area, porous, thermal and morphological properties of FPMBs. These types of FPMBs are useful in solid-phase synthesis, solid-phase extraction, and biomedical applications.

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