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Review Article

Spider silk: an excellent biomaterial for medical science and industry

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Abstract

Spider silk is categorized as fibrous protein. Spiders produce several types of silk. Spider silk is important because of its maximum mechanical strength, biocompatibility and biodegradability, pore filling ability and very low immunogenicity. In this review structure and types of silk producing gland, spinning process, chemistry of spider silk fiber, mechanical properties and applications of silk in health, military industry and many other fields is discussed. Its antifungal and antimicrobial potentials are also explored. Researchers are trying to introduce advanced methods to manufacture spider silk artificially to enhance silk production. Silk fiber can be designed after determining type and sequence of constituent amino acid or by inserting silk producing gene in another suitable animal.

Keywords: Silk, spiders, applications, mechanical properties, anti-microbial potentials

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INTRODUCTION

Spiders evolve about 374-380 million years ago and *Attercopus fimbriamguis* is known to be the oldest spider species (Selden *et al.,* 1991). At present, spiders constitutes a diverse group of 114 families, 3935 generas and 44,906 species occurring worldwide (Platnick, 2014). Spiders are ranked seventh according to their global diversity (Coddington and Levi, 1991). They are very cosmopolitan in their distribution and are widely dispersed in a range of habitats including polar areas as well as hot and dry environment e.g. in deserts (Foelix, 1996). Their maximum diversity is observed in tropical rain forests (Lamoral, 1968). Spiders play very essential part in our ecosystem and food chain. They are the major predators that naturally regulate and limit the pest populations of different crops (Mishra *et al*., 2012). Moreover, the spiders protect us from the mosquito borne diseases by feeding upon mosquitoes and their larvae (Vankhede, 2013).

Spiders are one of the most successful predators of pest and non-pest populations (Agnarsson *et al*., 2010). They are equipped with nature's wondrous material known as "Spider silk". The number of spider species that produce silk is around 41,000 (Agnarsson *et al*., 2010). The webs of spiders are specially fabricated to capture their prey. Their web is designed in such a way that allows spider to devour on a large variety of prey items. Ground spiders construct their webs on grounds and predate on crawling insects. While the other spiders have ariel traps specifically designed to capture flying insects. Apart from capturing prey the web of spiders are also a place of retreat that saves them from predators and external influences (Mishra *et al.*, 2012).

Each spider species produce different kind of web in accordance with the habitat, lifestyle and food availability. At a time more than one kind of silk can be produced by the spiders (Foelix, 1996). Orb-weaving spiders can produce up to seven different types of silk (Andersen, 1970). These different silk proteins have different properties and uses. Type of silk fiber formation depends upon spider requirement either it needs this silk fiber for food storage or to sense vibration in web lines to capture prey (Winkler and Kaplan, 2000; Hoefler, 2007). All of these web proteins are specific for their particular role e.g. aciniform

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silks are hardest spider silk type that help spiders to immobilize their prey (Liivak *et al*., 1997; Hayashi *et al*., 2004). Aciniform silks are also constituents of egg case silk of spiders. The presence of aciniform silks in egg sacs is not well defined but it may play an important role to control access of predators to the enclosed eggs. Flagelliform silks mainly present in orb-weavers, have maximum mechanical strength form spiral capture silk (Lewis, 2006). Spiral capture silk fibers are placed in orb webs to absorb and waste large amounts of mechanical energy introduced during the collision of aerial insects (Lin *et al*., 1995). Dragline silk is an extremely tough and elastic component in the web produced by major Ampullate gland. It is involved in the formation of orb web radii and frame. Glue-like silk produced by Aggregate gland functions in attachment and prey capture. Cocoon silk produced by cylindrical gland is utilized in reproduction and egg casing. Wrapping silk produced by Aciniform gland aids in wrapping of captured prey (Lewis, 2006).

Chemistry of spider silk fibers

Spider silk is categorized as fibrous protein having molecular weight>200 KDa (Vollrath, 1999; Altman *et al.,* 2003). Although the spiders can produce up to seven different kinds of silk yet some major constituent amino acids are similar (Work and Young, 1987; Craig, 1997). A primary building block of silk proteins constitutes of non-essential amino acids including Glycine and Alanine. Some other heavier amino acids present in silk proteins are arginine, serine, leucine, glutamine and tyrosine. These structural components are present in repetitive order (Craig and Riekel, 2002). The arrangement of these amino acids in various way along with the spinning process (Porter *et al.,* 2005) and the absorbed moisture (Altman *et al*., 2003; Blackledge *et al*., 2005), is responsible for unique properties of spider silk. Proteins present in silk exhibit different structural forms e.g. β-spirals, β-sheets and α- helices (Rising et al., 2005).β-sheets play an important role in enhancing stretching ability of fiber while β-spirals are involved in elastic property of silk (Kluge *et al*., 2008). Silks are organized from the basic structural unit (amino acid) (Craig & Riekel, 2002; Valluzzi *et al*., 2002) up to micro- and macroscopic structures (Hakimi *et al*., 2006). It has also been noted that spider silk also contain lipids such as 12-methyltetradecanoic acid and 14-methylhexadecanoic acid (Heimer, 1988; Schulz, 2001).

Silk glands and web spinning mechanism

The apparatus involved in silk formation is a small mechanical device that has evolved over millions of years (Romer and Scheibel, 2008). The silk production relies upon silk glands located at the posterior part of unsegmented abdomen. Solution of spider silk protein produced in silk gland is secreted and stored in the sac area of gland at protein concentrations up to 50% (w/v) (Hijirida *et al*., 1996). For producing different types of silk, spiders have seven different kinds of silk producing glands; these are the major and minor ampullate (used for locomotion and web frames), tubuliform (egg-case silk), flagelliform (capture spiral silk in orb-weaving spiders), aggregate (the glue in orb and cobwebs), pyriform (attachment disc for joining fibers) and aciniform (prey wrapping silk) (Guerette *et al*., 1996; Hsia *et al*., 2011; Hinman *et al*., 2000; Lewis, 2006). Silk proteins formed by these glands are different from each other as far as their mechanical, elastic, antimicrobial, antifungal and medical properties are concerned. The silk after being produced in silk glands is expelled outside through the distal openings of spinnerets known as spigots (Roberts, 1999). Spinnerets are microscopic tubes present at the posterior end of spider's abdomen following the silk glands (Lewis, 2006). They are directly involved in spinning and the extruding of silk fibers. They often exist in three or four pairs. Spinnerets are classified into anterior, median and posterior spinnerets (Roberts, 1999). Various spider species possess varied number and arrangement of these spinnerets (Yoshida, 1980). When a spider starts the spinning process, the state of silk protein becomes change from crystalline liquid to solid. Notable changes occur when silk solution passes from sac area to spinnerets by passing through a narrow tube. The structure of spider silk protein solution in the sac area is mainly alpha-helical or tangled (Hijirida *et al*., 1996; Dicko *et al*., 2004). During the passage through the spinning duct many changes occur e.g. variation in chemistry of ions, acidic pH mediated by carbonic anhydrase (Andersson *et al*., 2014), hydrogen bonds formation between the protein molecules (Scheibel, 2004) and loss of water. As a result of all these events alpha-helical structure of spider silk protein changes into beta-rich solid fiber (Dicko *et al*., 2004;

Romer and Scheibel, 2008; Vollrath and Knight, 2001). Then these beta sheets cross-linked to each other and attain solid structure (Scheibel, 2004). Solid state of silk consists of bundle of fibrils composed of crystalline or amorphous protein (Li *et al*., 2006; Buehler *et al*., 2008; Bourzac, 2015). A number of studies have shown a remarkable difference in properties of spider silk inside silk producing gland and when it comes out from spider body (Foelix, 1996). In its liquid form inside silk producing gland it is soluble but in solid form it becomes insoluble. In wet form it is lighter in weight. It has ten times lesser weight in liquid form than solid state (Foelix, 1996). The stretching ability of liquid form of spider silk is higher than dry form of silk (Foelix, 1996). Spinning and the associated material properties of silk fibers are usually affected by climatic temperature (Lin and Edmonds, 1997; Lin *et al*., 1995). Spiders often spin their webs at relatively high humidity and low temperature at early morning and in the evening (Yang *et al*., 2005).

Applications of spider silk

Spider silk is a commercially desired biomaterial due to possession of extraordinary properties such as high tensile strength, utmost elasticity and extreme hardness. The importance of spider silk was even realized in prehistoric times. Humans have been using it for thousands of years for various purposes. They exploit it for wound healing, fishing, making bags and clothes (Altman *et al*., 2003). Historically, ancient Greek utilized spider webs to dress wounds owing to its low immune stimulatory effect and enrichment of vitamin K (Newman and Newman, 1995). In native Solomon Islands spider silk is largely utilized in making of fishing lines (Heim *et al*., 2009). Owing to elastic nature and high strength of silk fiber it can prove a valuable construction material in earthquake proof houses (Vankhede, 2013). Silk fibers having high safety coefficients can find applications in manufacturing of ropes for elevators, bridges and pillars (Osaki, 1999).

Spider silk can be used in cosmetics to improve the softness and brightness of products (Vendrely and Scheibel, 2007). Cobwebs of spiders can also be utilized for estimation of industrial as well as residential area pollution (Ayedun *et al*., 2013; Hose *et al*., 2002). Moreover, birds use to line their nest internally with spider silk. This lining provides smooth texture to the nest and prevents infections due to its antibacterial nature (Vankhede, 2013). The spider silk is also used in manufacturing of rust free panels on boats and motor vehicles. Furthermore, biodegradable bottles, bandages and surgical thread could also be the possible items made out of the spider silk (Singha *et al*., 2012). At present, spider silk is in current focus of interest as it exhibits unique structural, mechanical, bio-medical, bio-engineering and therapeutic applications

Mechanical properties of spider silk

Spider silk possess remarkable mechanical properties. It is a unique blend of high tensile strength and extensibility. Spider silk is tough (Gosline *et al*., 1999; Osaki, 2012). It is five times stronger than steel and two times that of Kevlar (Vollrath and Knight, 2001; Ko *et al*., 2001). It is hardest material known to-date because of its maximum load bearing ability and elasticity (Bourzac, 2015). Some spider silk types can extend to 140% of their original length without breaking (Vollrath and Knight 2001).

The mechanical properties of silk fibers spun by spiders vary depending on many extrinsic and intrinsic factors (Hu *et al*., 2006). The factors involved in determining strength and load tolerance response of silk fibers mainly include heat, moisture, and exit rate. Mechanical properties of spider silk also depend upon the way of spinning as well as chemistry of constituent amino acids (Work and Young 1987; Craig 1997; Vollrath and Knight, 2001). Correlations between the wind speed and the stretching abilities of dragline silk fibers have been observed experimentally, supporting that spiders can adjust their thread properties by changing the exit rate from their spinnerets. Actually the stretching ability and wind speed controls the size of beta-sheet crystallite (Du *et al*., 2006). The polypeptides of silk fibers have 3 nm beta-sheet crystallite posses maximum stretching strength. Many studies reported that nanocrystals of this size are actually present in natural dragline silk (Nova *et al*., 2010).

Load-deformation response of Dragline silk fibers, aciniform silks (Hayashi *et al*., 2004), tubuliform silks (Hu *et al*., 2006), flagelliform silks (Lewis, 2006) and minor ampullate silks (Liivak *et al*., 1997) was compared by many researchers and it was observed that spider dragline silk has maximum mechanical strength (Hinman *et al*., 2000). Its load tolerance ability is equivalent to that of the artificial polymer Kevlar and stronger than tendons (Hinman *et al*., 2000; Vollrath and Knight 2001). These mechanical properties can be correlated with its composition. It maximum tensile strength is because of polyalanine segments while extensibility of the fibers is due to glycine-rich regions (Simmons *et al*., 1996). Moreover, the spider silk holds its mechanical toughness over a broad range of temperatures i.e. -66 to 100°C. Also the strength of silk fiber increases remarkably by lowering the temperature (Yang *et al.,* 2005;Pogozelski *et al.,* 2011).Studies have shown that at very low temperature (-196 °C) strength of fiber enhanced by 64% as compared to strength at room temperature (Pogozelski *et al*., 2011). Possession of the unique and extraordinary mechanical properties makes spider silk far more superior than the man-made artificial fibers.

The most studied silk concerning the remarkable mechanical properties is the dragline silk. Dragline silkis used by spiders to form their safety line (Benjamin and Zschokke, 2004). *I*t also forms the basic framework and backbone for most of the webs (Blackledge *et al*., 2005; Coddington, 1989). It is spun by major ampullate glands (Vollrath and Knight 2001). This gland has two main parts; a long tail and a wider sac area (Vollrath and Knight 2001). Many scientists have tried to expose the chemistry of dragline silk. The studies reveal that the *d*ragline silk consist of four layers including the inner core, skin and the outer glycoprotein and lipid layer (Sponner *et al.*, 2005). *D*ragline silk is a complex material mainly made up of two constituent proteins named as MaSp1 and MaSp2 (Humenik *et al*., 2011), some other molecules present in living organisms like glycoprotein and lipids (Tokareva, 2014). Three to five (3-5) disulfide bonds near their carbonyl-termini are responsible for connection of these two proteins (Bini *et al*., 2006). Spider silk has muco-polysaccharide (highly viscous in nature) on surface of silk (Casem *et al*., 2002; Sponner *et al*., 2005). Role of muco-polysaccharide is still unknown. The toughness and mechanical strength of spider silk is due to the presence of heavy aromatic benzene ring in non-essential aminoacids i.e. Alanine and Glycine (Riekel and Vollrath, 2001).

Biocompatibility and medical applications of spider silk

One of the most important and astonishing discovery about spider silk is its biocompatibility to the living tissues of human beings. This potential of spider silk was also studied in many other animals e.g. in pigs (Vollrath *et al*., 2002), mice and rats (Gellynck *et al*., 2008). In these animals implantation was done successfully under their skin. The results of these experiments were very surprising because their immune system did not recognize it as foreign body and no inflammatory response was observed. These studies also made it clear that the spider silk especially native drag-line silks does not induce any kind of rejection in the living tissues. So the drag-line silk can be used in vast therapeutical and medical applications. Another important characteristic of spider dragline silk is its stability even at high temperature. It can tolerate very high temperature without any change in its chemistry. These silk fibers maintain their appearance, anatomy and stretching capabilities even when autoclaved (Hedhammar *et al*., 2010). This property enhances its use in therapeutics (Gellynck *et al*., 2008).

This renders spider silk as a worthy contender for advanced anti-microbial drug development. Although, the anti-microbial compounds of spider silk have created the hope for the effective treatment of emerging bacterial infections. Yet, addressing the safety concerns of new therapies on biological systems is currently needed. Although many of the tested spider silk fibers are biocompatible and mild arrangement of amino acids in various kinds of spider protein is different, so before use its biocompatibility must be evaluated. All types of spidrion fibers are not equally biocompatible (Gellynck *et al*., 2008).

Wound repairing and regenerating potential

Applications of spider silk in medical field and life-sciences is increasing nowadays (Altman *et al*., 2003; Bourzac, 2015). Spider silk possess outstanding and valuable therapeutic, wound healing and regenerative properties (Shear *et al*., 1989; Seenivasan *et al*., 2005). This makes spider silk a remarkable and extraordinary biomaterial (Gosline *et al*., 1999; Vollrath, 2000). Spider silk play important role in the regeneration of many tissues and body cells such as skin, nerve, bone, and cartilage (Altman *et al*., 2003; Schneider *et al*., 2009; Sionkowska, 2011; Wendt *et al*., 2011). Many damaged connective tissues such as tendons and ligaments can also be repaired (Schneider *et al*., 2009; Hennecke *et al.,* 2013; Bourzac, 2015). Spider silk films supply structural support and induces regeneration in the tissues (Sionkowska, 2011).

Regeneration of nerve cells

Silk fiber can also be used to treat nerve disorders. As the major ampullate silk fibers show biocompatibility and very low immunogenicity when grown with Schwann cells (nerve cells) of human being (Allmeling *et al*., 2006). Different classes of artificially designed polymers such as poly-glycolic acid (PGA) and poly L-lactic acid (PLLA) have been studied in detail in order to treat various diseases of nervous system but these experiments failed to attain desirable results because of very intricate system and structure of nerves but spider silk was found to be involved in myelin formation, regeneration of damaged axonal cells, movement of Schwann cells in nerve, and betterment of nerve impulse transfer (Radtke *et al*., 2011; Tokareva *et al*., 2014). *Nephila clavipes* silk has been reported to be involved in regeneration of neuronal cells of mammals (Allmeling *et al*., 2006). It also provides structural support and site for attachment to cells of connective tissue and keratin producing epidermal cells (Wendt *et al*., 2011). So spider silk fibers play very important role in healing of injury because it improves the regeneration of damaged cells.

Scaffolds and prosthesis

Due to biocompatibility and enduring nature of spider silk it can find applications in formation of artificial muscles, tendons and ligaments. Current studies have also revealed that the spider silk (*Nephila edulis* egg cases) can be used for engineering of supporting structures that assist and support the chondrocytes (cartilage tissues) (MacIntosh *et al*., 2004). After some successive attempts porous scaffolds resembling hyaline cartilage were successfully engineered from spider silk fibers. These scaffolds seemed to support chondrocyte adherence and propagation (Gellynck *et al*., 2005). Spidroin play an important role in engineering of these scaffolds because its mechanical characteristics are similar to that of natural chondrocytes (Bai *et al*., 2006). Spider silk can also be used to make the long-lasting implants. These days the silk made prosthesis supporting fracture bones are on way of development. Spider silk when used in making implants and prosthesis not only support the affected area but also induces healing and regenerative effects in living tissues (Bai *et al*., 2006). Moreover due to its biodegradable nature it degrades naturally inside the body without need of removing it by surgical process.

Textile and military applications

Spider silk finds a number of applications in military and textile industries due to its versatile attributes of great strength and remarkable flexibility. Spider silk has been used until World War II as cross-hairs in optical devices such as telescope, microscopes and bomb guiding artifacts (Ricki, 1996). Spider silk due to its super toughness is capable of devising replacement material for various merchandises including body amours, bullet proof clothing, seat belts, ropes and nets. The spider silk possess an extraordinary property of dissipating energy at high strain rate, thus can be used as a ballistic protector (Cunnif *et al*., 1994). Also, the super tough fibers made out of spider silk can be used in fabricating the parachute and its ropes (Gerritsen, 2000). In textile industries the spider silk can be used in production of wear-resistant lightweight clothing. Another possible application of spider silk is in manufacturing of sport goods (Service, 2002). As spider silk is strong and load bearing biomaterial, thus it can be used in construction of bridges, rust-free panels of motor vehicles and even aircrafts bodies (Brown *et al*., 2011). Spider silk can also be largely used in bags and cloth construction (Berenbaum, 1995).

Antimicrobial potential

Currently, the dilemma of emerging multi-drug resistant pathogens is of great concern. The problem is rooted in the overuse and misuse of broad spectrum antibiotics (Zuridah *et al*., 2008). Today, the medical and pharmaceutical industries are drudging hard to develop an effective treatment against the prevailing infectious maladies. In this aspect the anti-microbials derived from natural sources always surpass the synthetics because they include effective and bio-friendly therapeutic substances. Moreover, they present a natural mean of restricting microbial growth and with the less chance of pathogens to acquire resistance against them (Craig *et al*., 1997).

Thus in this present age of alarming health concerns the spider silk could prove a miraculous substance having potent antibacterial activity. The lipids present in spider silk contain 12-methyltetradecanoic acid and 14-methylhexadecanoic acid that inhibit growth of microbes (Heimer, 1988). Many other studies have also exposed that 12-methyltetradecanoic acid prevent the growth of rice pathogen, *Magnaporthe oryzae* (Pohl *et al*., 2011). Therefore, spider silk is gaining attention and scientists are trying to expose its anti-microbial properties. Heimer (1988) first time observed that micro-organisms are unable to grow on spider silk because of its acidic nature. Anti-microbial activity observed in all these studies was because of soluble/ non-soluble growth restraining factors in silk (Suto *et al*., 1992) or surface or structural property of a material (Bhushan, 2011).

Silk fibers from aciniform and tubuliform gland were examined. It was found that they possess two small coating peptides SCP-1 and SCP-2. These two peptides may be involved in anti-microbial role of silk (Hsia *et al*., 2011). Also, the antimicrobial properties of *Tegenaria domestica* silk were assessed by some researchers (Border, 2001; Chakraborty and Das, 2009). Wright and Goodacre (2012) reported that spider silk has anti-microbial activity against *Bacillus subtilis* (Gram negative bacteria) but no bacteriostatic action was observed for Gram negative bacteria *(Escherichia coli*). Bacteriostatic is an organic substance that prevents bacteria to grow and reproduce (Pankey and Sabath, 2004). Furthermore, the web of *Nephila antipodiana* (orb web spider) contains a chemical insecticide 2-pyrrrolidinone (an acid derivative) that was very helpful to inhibit the attack of ants on web. This chemical is not an extra product of silk but spider produces it actively for self defense (Zhang *et al*., 2012). This indicates that spiders have ability to protect themselves from natural enemies. Spider has ability to preserve its extra food for months and even years by folding it in silk fibers. This stored food is safe from attack of fungus or other microbes (Eberhard *et al*., 2006). Spider gains this benefit of their silk because of chemical compounds present in it (Roozbahani *et al*., 2014). These anti-microbial compounds are amino acids such as glycine, alanine and huge quantity of pyrrolidine in silk fiber. Amino acids prevent the silk fibers from drying by tending to absorb moisture from the air. Anti-fungal and anti-microbial compounds such as bisphosphonates peptides, phospholipids hydrate and potassium nitrate were also observed in silk fibers (Chakraborty and Das, 2009; Gomes *et al*., 2010). Tahir *et al.* (2015) reported that silk of *Neoscona theisi*inhibit growth of fungus on bread. These all chemical elements present in silk are very important in enhancing the economy of country because these kill those microbes that are damaging crops, fruits, decomposing food above threshold level and also dispersing many epidemic disorders (Roozbahani *et al*., 2014). These anti-microbial compounds basically induce growth inhibition zone in both gram positive and gram negative bacteria i.e., *Listeria monocytogenes* and *Escherichia coli* (Roozbahani *et al*., 2014). In another study it was observed that Gram positive bacteria are more susceptible than gram negative bacteria by spider silk when its growth inhibition effect was determined (Mirghani *et al*., 2012). The role of spider silk to kill microorganisms was also reported by Chakraborty and Das (2009) and Wright and Goodacre (2012).

Mechanism of action of potassium hydrogen phosphate was studied in detail. It was observed that this antimicrobial peptide create an acidic environment with pH of about 4 by releasing protons in aqueous medium (Heimer, 1988). Acidic conditions are not suitable for growth of fungus and many pathogenic and silk protein digesting bacteria therefore this silk is protected from bacterial attack. Potassium nitrate in spider silk also inhibits bacterial growth and hence protects silk from degradation (Heimer, 1988). So spider silk can be used to store and preserve food. Also, a protein was discovered in spider silk that is able to stabilize temperature sensitive biological products used for therapeutic purpose for months at room temperatures or even in warmer conditions (Zhang *et al*., 2012). So it is an important discovery that makes possible the transportation and maintenance of temperature-sensitive medicines, vaccines and other food products (Lammel *et al*., 2010).

Commercial production and limitations

There is no doubt in the importance of spider silk. A range of characteristics were observed in silk fiber such as remarkable mechanical strength, toughness, hardness, extensibility, capability of being decomposed by bacteria and other living organisms, and suitable processing conditions (Rising, 2014) that make it a very useful material (Bittencourt *et al*., 2012). Applications and uses of spider silk in various fields especially medical, industrial, and armed services is increasing day by day (Lammel *et al*., 2011). But there are many problems for production of spider silk at commercial and industrial level. First of all very low amount of silk can be obtained by spider, 400 spiders will produce only one square yard of cloth (Altman *et al*., 2003; Hakimi *et al*., 2007). It is very difficult to rear raise spiders because of their cannibalistic behavior (Andrade, 1988). When silk comes out from spider body it solidifies so it is difficult to further process it (Hakimi *et al*., 2007). Many advanced methods to manufacture spider silk artificially are under consideration (Scheibel, 2004). There are basically two ways to obtain spider silk artificially; one is to design it after finding chemistry and sequence of constituent amino acids and second method is to recognize spider gene actually involving in synthesis of spider silk protein then isolating and inserting it in another host organism (Teule *et al*., 2009). Recombinant spidroin are important to build biofilms (Bini *et al*., 2006) as well as hydrogels that will not deteriorate over a few weeks (Rammensee *et al*., 2006).

Another process of silk collection is called forced silking. In this method the spider is kept motionless and is forced to produce silk. The silk fibers are obtained by simulating spiders. The silk produced by controlled spinning is gathered through the rotating cylinder (Ortlepp and Gosline, 2004; Elices *et al*., 2005; Perz-Rigueiro *et al*., 2005). Although in this method pure and natural silk is obtained yet low production rate is one of biggest limitation of this process .Thus it cannot be used at industrial level.

Spider silk in finest form is very costly so, it is mixed with less expensive synthetic polymers to minimize the price of the biomaterials (Sionkowska, 2011). As spiders produce silk in a very low quantity so to fulfill the needs and overcome this problem there is a dire need to produce it artificially (Lammel *et al*., 2011). Amino acid type and sequence was determined to design spidroin fiber. Development and progress in molecular biotechnology has made it possible to get spider silk protein in sufficient quantity. Recombinant dragline silk fibers were synthesized and their biocompatibility was assessed in mouse fibroblast cells. This study implying best results showing that recombinant dragline silk fibers have remarkable biocompatibility, strength and pore filling ability (Agapov *et al*., 2009). Artificially designed spider silk proteins were also successfully used as biomaterial matrixes to increase the differentiation of human bone marrow derived mesenchymal stem cells to bone-like tissue (Bini *et al*., 2006; Wendt *et al*., 2011). Although the spider silk has proven to be a miraculous substance having a wide array of applications yet addressing the safety concerns on biological systems is currently needed.

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