International Journal of Pharmacology and Clinical Research
Online ISSN: 2664-7621; Print ISSN: 2664-7613
Received: 01-03-2019; Accepted: 03-04-2019; Published: 10-04-2019
www.pharmacologyjournal.in
Volume 1; Issue 1; 2019; Page No. 25-28

Environmental sources of contagious prion proteins

Prabhu K Das[1], Bibhuti P Barik[2]
[1-2] PG Department of Zoology Khallikote Autonomous College, Berhampur, Odisha, India

Abstract
Prions are cellular proteins with neuroprotective functions. These are found in many tissues but are highly expressed in central nervous system. Sometimes these proteins are misfolded after translation resulting in neurodegenerative diseases. These disorders are observed in a number of species including humans. In prion disorders the misfolded proteins assemble at the synapse terminals resulting in synaptic loss. This may turn fatal for any organism. Contagious forms of these proteins enter the environment through the excreta, blood or other secretion of infected organisms. These proteins can thrive in the environment for several years without any change in their tendency of infection. These can transmit through soil and water. These proteins become more infectious upon binding with the soil minerals. The inter-specific infection capability makes these proteins more harmful. People who consume red meat may get infected with prion proteins. This is a mini review highlighting environmental sources of the contagious prion proteins.

Keywords: prions, neurodegenerative disorders, environment, soil, water, plant

Introduction
Proteins are one of the important biomolecules in living organisms. These constitute approximately 20% of the human body which are vital morphological, anatomical, physiological, and genetical point of views. Several proteins work according to their requirements in the body to maintain a proper physiological condition. But these can prompt harmful impacts upon malfunction or when present in abnormal structural conformation. Prion proteins are cellular proteins (PrP^{C}) with neuroprotective functions [1]. Cellular prion proteins are abundant at axonal terminals [2]. Except nervous system it is also expressed in several other tissues. The gene PRNP encoding the cellular prion protein is located on chromosome number 20. These proteins are converted to their abnormal protease resistant forms (PrP^{Res}) [3]. These include scrapie forms of prion proteins (PrP^{Sc}), which result in disorders. These are considered as autoimmune disorders because antibodies acting against PrP^{Sc} are reported to alter PrP^{C} into PrP^{Sc} [4]. In neurodegenerative disorders, these misfolded proteins (PrP^{Sc}) are aggregated in the synapse terminals and results in synaptic disorganization [5]. Diseases related to misfolded prion proteins are called transmissible spongiform encephalopathies (TSEs). These neurodegenerative disorders affect several species. There is not any nucleic acid coupled with the causative agent of these diseases [6].

Prion proteins
Prion proteins are highly conserved in mammals. Gene PRNP encodes the normal cellular prion protein (PrP^{C}). PrP^{C} can alter into its contagious isoform PrP^{Sc}.[7] Contagious forms of prions polymerize into amyloid at the synaptic cleft resulting in synaptic loss. But the transformation of PrP^{C} into PrP^{Sc} is not always the cause of the disease [8]. PrP^{Sc} molecule is about 33–35 kDa [9]. These proteins have several isoforms with different structural conformations of PrP^{Sc} [10]. Amino acid sequences of PrP^{Sc} and PrP^{C} are equal but differ in their structural conformations. PrP^{C} is rich in α-helices and lacks β-sheets but PrP^{Sc} have more β-sheets and less α-helices [11]. Proteins have specific glycosylation patterns. Hence glycosylation patterns may categorize different prion strains [12]. Prions can replicate themselves in suitable medium [13].

Prion related ailments in mammals
Nervous system in animals is vital in control and coordination. Any malfunction in this system can be deadly for any organism. Misfolded prion aggregation in synaptic junctions causes neurodegerative disorders, otherwise called as transmissible spongiform encephalopathies (TSEs). In cattle these are called bovine spongiform encephalopathy (BSE), scrapie in goats and sheep, transmissible mink encephalopathy (TME) in farmed mink and chronic wasting disease (CWD) in cervids. In infected organisms elevated level of prion proteins are accumulated in the central nervous system. In human beings TSEs involve ailments like; kuru, Creutzfeldt-Jakob disease (CJD), variant Creutzfeldt-Jakob disease (vCJD), Gerstmann-Sträussler-Scheinker syndrome (GSS),fatal familial insomnia (FFI), etc[14]. Mutations in human PRNP gene cause most of these diseases [15].

Access of PrP^{Sc} into the surroundings of exposed animals
In the natural environment PrP^{Sc} retain their contagious characteristics for several years. Scrapie forms of prions can transmit upon introduction of infected animals to farms which are not exposed to scrapie previously [16]. Skin, skeletal muscle, saliva, blood, milk, nasal secretions, urine, faecal matter and even placenta of infected organisms carry prion proteins [17-21]. Prions are found in the external secretions of

infected organisms, many months prior to the appearance of the symptoms of the disease [22]. Following the putrefaction of the dead bodies of infected animals, prions enter into the environment [23].

Environmental sources of prion proteins

There are three possible ecological reservoirs for prions; soil profile, water bodies, and plants. Furthermore mineral licks and bedding sites are the possible reservoirs of scrapie prion proteins [24]. Carnivores and scavengers those consume meat of infected organisms are possible carriers of misfolded prion proteins.

i. Soil

Soil is an important reservoir of prions resulting TSE [25], although it is assumed that soil microbes are having the capability to alter these abnormal proteins into their inactivate forms [26]. Prions present in the discharges of infected organisms, interact with soil particles [27]. Prions can easily bind to soil since these have a strong affinity towards quartz sands and minerals in the clay [28]. These contagious prion proteins are transmitted to the ruminants during grazing [29]. CWD prions bound to dust particles transmit to deers through nasal openings [30]. Soil mineral coupled prion proteins can possibly resist the effect digestive enzymes in ruminants. Prions in complex biological materials, take more time to interact with soil than the prions in simple materials [31]. Affinity of different PrP^{Sc} strains to soil is variable. Recombinant prion proteins have more affinity for organic materials [32]. Prions can migrate through the soil profile [33]. Hamster-adapted transmissible mink encephalopathy prions have strong affinity for soil minerals [34]. The clay-bound proteins are more contagious than the free protein [35]. PrPC turns into its contagious form after binding to a soil mineral i.e. montmorillonite (MTE) [36]. Adsorption of PrP^{Sc} to soil particles is almost unalterable [37]. Soil and clay mineral bound prions are more stable and contagious but unbound prions degrade after a certain period [38].

ii. Water

The prions possibly can interact with surface or ground water. Prions those migrate through the soil can possibly penetrate the water line. The plants exposed to the wastewater runoff from slaughterhouse uptake PrP^{Sc} and can infect herbivores those consume these plant products [39]. Prion proteins have been isolated during wastewater treatments [40]. Protease resistant CWD prion proteins are found in water samples suggesting its possible transmission through water [41]. Infectivity and degradation of PrP^{Res} were moderately prohibited by the organic materials in water [42]. Tendency of infectivity in prion proteins related to BSE was declined negligibly in raw sewage [43]. CWD from affected deer can transmit through water to unaffected deers[44]. Several animal species are exposed to these water containing contagious prion proteins. They may also get infected and transmit these to unaffected organisms in turn. More work regarding the binding of prion proteins to soil particles have been recorded. But there is less evidence about prion protein interaction with water.

iii. Plants

Plants are an important component in diet for diverse group of organisms including human beings. Plants receive proteins through roots and other tissues as a resource of nitrogen [45]. PrP^{Sc} present in the ground water can be absorbed by the root system of wheat grass [46]. Hence misfolded prions can enter plant body during osmosis through root systems from soil. It has been observed that plants like *Triticum aestivum* and *Hordeum vulgar* grown in soil tainted with high concentrations of prion proteins can uptake prions into their root, stem, and leaves [47]. Plants having underground modified parts probably get affected the most. These parts are consumed by many organisms including human. Grass and other plant materials containing prion proteins are consumed by the herbivores and they get infected.

Transmission of prion proteins

PrPSc has unique characteristics like proteolytic resistance, hydrophobicity and a tendency for augmentation [48]. Different prion strains infect different species [49]. Prion disorders are transmitted through oral consumption [50] of the contagious prions present in several organic materials and sometimes through nasal cavity [51]. These prions reach small intestine surviving the harsh environment [52]. In ileum, prions interact with lymphoid tissue and enter the Peyer's patches to reach the central nervous system [53, 54]. CJD can be transmitted during pituitary hormone treatments, duramater grafts, corneal grafts and blood transfusions [55]. TSE communication is not species specific [56]. Consuming infected red meat may cause these proteins to transmit [57]. Disorders like scrapie and CWD are having species specific transmission [58].

Measures of prion degradation

The potency of these proteins to thrive in the environment for years makes them more harmful as they can continuously affect several generations. Hence proper degradation of these proteins in the environment is necessary. In the environment, prion can be disintegrated through burning the specified risk materials, specific chemical treatments and composting. Prions disintegrate in extreme climate like excess temperature, dry, and wet conditions [59]. Microbes in soil and lichens are capable of degrading contagious prion proteins in their surroundings [60]. Ozone treatment work significantly for prion oxidation to reduce infectivity in and specified risk materials (SRM) and contaminated waste water [61].

Conclusion

Prion proteins causing TSE can be transmitted to an organism in every possible way. TSE are a group of dangerous diseases appearing in several species including human beings. These are hazardous inter-specific communicable disorders. These mostly occur due to abnormal conformation of PrP^{C}. These infected protein forms can survive any extreme environmental condition for several years without losing their tendency to infect other animals exposed to them. These can migrate through soil profile and possibly through water. The natural environment is a vital source of these proteins. Consuming red meat infected with these proteins can also transmit these disorders. There are treatment measures for these neurodegenerative disorders but the diagnosis of these

ailments is very important as the affected organisms start to release misfolded prions through their external secretions. There are no certain precautions for these disorders. Therefore more efforts should be put on the proper disposal of the carcass of infected organisms and specified risk materials.

References

1. Williams SK, Fairless R, Weise J, Kalinke U, Schulz-Schaeffer W, Diem R. *et al*. Neuroprotective effects of the cellular prion protein in autoimmune optic neuritis. Am J Pathol, 2011; 178:2823-31.
2. Moya KL, Sales N, Hassig R, Creminon C, Grassi J, Giamberardino Di L. *et al*. Immunolocalization of the cellular prion protein in normal brain. Microsc Res Tech, 2000; 50:58-65.
3. Prusiner SB. Novel proteinaceous infectious particles cause scrapie. Science, 1982; 216:136-44.
4. Liberski PP, Brown DR, Sikorska B, Caughey B, Brown P. Cell death and autophagy in prion diseases (transmissible spongiform encephalopathies). Folia Neuropathol, 2008; 46:1-25.
5. Jeffrey M, Halliday WG, Bell J, Johnston AR, MacLeod NK, Ingham C. *et al*. Synapse loss associated with abnormal PrP precedes neuronal degeneration in the scrapie-infected murine hippocampus. Neuropathol Appl Neurobiol, 2000; 26:41-54.
6. Deleault NR, Harris BT, Rees JR, Supattapone S. Formation of native prions from minimal components in vitro. Proc Natl Acad Sci, USA, 2007; 104:9741-46.
7. Kim JI. Mammalian prions generated from bacterially expressed prion protein in the absence of any mammalian cofactors. J Biol Chem, 2010; 285:14083-87.
8. Chiesa R, Restelli E, Comerio L, Gallo FD, Imeri L. Transgenic mice recapitulate the phenotypic heterogeneity of genetic prion diseases without developing prion infectivity: Role of intracellular PrP retention in neurotoxicity. Prion, 2016; 10:93-102.
9. Oesch B, Westaway D, Wälchli M, McKinley MP, Kent SBH, Aebersold R. *et al*. A cellular gene encodes scrapie PrP 27-30 protein. Cell, 1985; 40:735-46.
10. Castilla Jn, Morales R, Saa P, Barria M, Gambetti P, Soto C. *et al* Cell-free propagation of prion strains. EMBO J, 2008; 27:2557-66.
11. Pan KM, Baldwin M, Nguyen J, Gasset M, Serban A, Groth D, *et al*. Conversion of α -helices into β-sheets features in the formation of the scrapie prion proteins. Proc Natl Acad Sci, USA, 1993; 90:10962-66.
12. Collinge J, Sidle KCL, Meads J, Ironside J, Hill AF. Molecular analysis of prion strain variation and the aetiology of "new variant" CJD. Nature, 1996; 383:685-90.
13. Griffith JS. Nature of scrapie agent: Self-replication and scrapie. Nature, 1967; 215:1043-44.
14. Prusiner SB. Neurodegenerative diseases and prions. N Engl J Med, 2001; 344:1516-26.
15. Schmitz M, Dittmar K, Llorens F, Gelpi E, Ferrer I, Schulz-Schaeffer WJ. *et al*. Hereditary human prion diseases: An update. Mol Neurobiol, 2017; 54:4138-49.
16. Georgsson G, Sigurdarson S, Brown P. Infectious agent of sheep scrapie may persist in the environment for at least 16 years. J Gen Virol, 2006; 87:3737-40.
17. Angers RC, Browning SR, Seward T, Sigurdarson CJ, Miller MW, Hoover EA. *et al*. Prions in skeletal muscles of deer with chronic wasting disease. Science, 2006; 311:1117.
18. Mathiason CK, Powers JG, Dahmes SJ, Osborn DA, Miller KV, Warren RJ. *et al*. Infectious prions in the saliva and blood of deer with chronic wasting disease. Science, 2006; 314:133-36.
19. Gregori L, Kovacs GG, Alexeeva I, Budka H, Rohwer RG. Excretion of transmissible spongiform encephalopathy infectivity in urine. Emerg Infect Dis, 2008; 14:1406-12.
20. Safar JG, Lessard P, Tamgüney G, Freyman Y, Deering C, Letessier F. *et al*. Transmission and detection of prions in feces. Journal of Infectious Diseases, 2008; 198:81-9.
21. Maddison BC, Baker CA, Rees HC, Terry LA, Thorne L, Bellworthy SJ. *et al*. Prions are secreted in milk from clinically normal scrapie-exposed sheep. Journal of Virology, 2009; 83:8293-96.
22. Tamgüney G, Miller MW, Wolfe LL, Sirochman TM, Glidden DV, Palmer C. *et al*. Asymptomatic deer excrete infectious prions in faeces. Nature, 2009; 461:529-32.
23. Miller MW, Williams ES, Hobbs NT, Wolfe LL. Environmental sources of prion transmission in mule deer. Emerg Infect Dis, 2004; 10:1003-06.
24. Maddison BC, Baker CA, Terry LA, Bellworthy SJ, Thorne L, Rees HC. *et al*. Environmental sources of scrapie prions. J Virol, 2010; 84:11560-62.
25. Schramm PT, Johnson CJ, McKenzie D, Aiken JM, Pedersen JA. Potential role of soil in the transmission of prion disease. Rev Mineral Geochem, 2006; 64:135-52.
26. Booth CJ, Johnson CJ and Pedersen JA. Review: microbial and enzymatic inactivation of prions in soil environments. Soil Biol Biochem, 2013; 59:1-15.
27. Ma X, Benson CH, McKenzie D, Aiken JM, Pedersen JA. Adsorption of pathogenic prion protein to quartz sand. Environ Sci Technol, 2007; 41:2324-30.
28. Polano M, Anselmi C, Leita L, Negro A, Nobili MD. Organic polyanions act as complexants of prion protein in soil. Biochem Biophys Res Com, 2008; 367:323-29.
29. Seidel B, Thomzig A, Buschmann A, Groschup MH, Peters R, Beekes M. *et al*. Scrapie agent (strain 263K) can transmit disease via the oral route after persistence in soil over years. PLoS ONE, 2007; 2:e435.
30. Nichols TA, Spraker TR, Rigg TD, Meyerett-Reid C, Hoover C, Michel B, *et al*. Intranasal inoculation of white-tailed deer (*Odocoileus virginianus*) with lyophilized chronic wasting disease prion particulate complexed to montmorillonite clay. PLoS One, 2013; 8:e62455.
31. Saunders SE, Bartz JC, Bartelt Hunt SL. Influence of prion strain on prion protein adsorption to soil in a competitive matrix. Environ Sci Technol, 2009; 43:5242-48.
32. Saunders SE, Bartelt-Hunt SL, Bartz JC. Prions in the environment: Occurrence, fate, and mitigation. Prion, 2008; 2:162-69.
33. Cooke CM, Shaw G. Fate of prions in soil: longevity and migration of recPrP in soil columns. Soil Biol Biochem,

2007; 39:1181-91.
34. Johnson CJ, Pedersen JA, Chappell RJ, McKenzie D, Aiken JM. Oral transmissibility of prion disease is enhanced by binding to soil particles. PLoS Pathogens, 2007; 3:e93.
35. Johnson CJ, Phillips KE, Schramm PT, McKenzie D, Aiken JM, Pedersen JA. *et al*. Prions adhere to soil minerals and remain infectious. PLoS Pathog, 2006; 2:e32.
36. Revault M, Quiquampoix H, Baron MH, Noinville S. Fate of prions in soil: trapped conformation of full-length ovine prion protein induced by adsorption on clays. Biochim Biophys Acta, 2005; 1724:367-74.
37. Leita L, Fornasier F, Nobili MD, Bertoli A, Genovesi S, Sequi P. *et al*. Interactions of prion proteins with soil. Soil Biol Biochem, 2006; 38:1638-44.
38. Saunders SE, Shikiya RA, Langenfeld K, Bartelt Hunt SL, Bartz JC. Replication efficiency of soil-bound prions varies with soil type. J Virol, 2011; 85:5476-82.
39. Adkin A, Donaldson N, Kelly L. A quantitative assessment of the prion risk associated with wastewater from carcass-handling facilities. Risk Anal, 2013; 33:1212-27.
40. Hinckley GT, Johnson CJ, Jacobson KT, Bartholomay C, McMahon KD, McKenzie D. *et al*. Persistence of pathogenic prion protein during simulated wastewater treatment processes. Environ Sci Technol, 2008; 42:5254-59.
41. Nichols TA, Pulford B, Wyckoff AC, Meyerett C, Michel B, Gertig K. *et al*. Detection of protease-resistant cervid prion protein in water from a CWD-endemic area. Prion, 2009; 3:171-83.
42. Miles SL, Takizawa K, Gerba CP, Pepper IL. Survival of infectious prions in water. J Environ Sci Health A Tox Hazard Subst Environ Eng, 2011; 46:938-43.
43. Maluquer de, Motes C, Espinosa JC, Esteban A, Calvo M, Gironés R. *et al*. Persistence of the bovine spongiform encephalopathy infectious agent in sewage. Environ Res 2012; 117:1-7.
44. Mathiason CK, Hays SA, Powers J, Hayes-Klug J, Langenberg J, Dahmes SJ. *et al*. Infectious prions in pre-clinical deer and transmission of chronic wasting disease solely by environmental exposure. PLoS One, 2009; 4:e5916.
45. Rasmussen J, Gilroyed BH, Reuter T, Badea A, Eudes F, Graf R. *et al*. Protein can be taken up by damaged wheat roots and transported to the stem. J Plant Biol, 2015; 58:1-7.
46. Rasmussen J, Gilroyed BH, Reuter T, Dudas S, Neumann NF, Balachandran A. *et al*. Can plants serve as a vector for prions causing chronic wasting disease? Prion, 2014; 8:136-42.
47. Pritzkow S, Morales R, Moda F, Khan U, Telling GC, Hoover E. *et al*. Grass plants bind, retain, uptake, and transport infectious prions. Cell Rep, 2015; 11:1168-75.
48. Taylor DM. Inactivation of transmissible degenerative encephalopathy agents: a review. Vet J 2000; 159:10-17.
49. Raymond GJ, Raymond LD, Meade White KD, Hughson AG, Favara C, Gardner D. *et al*. Transmission and adaptation of chronic wasting disease to hamsters and transgenic mice: evidence for strains. J Virol, 2007; 81:4305-14.
50. Brown P, Brandel JP, Sato T, Nakamura Y, MacKenzie J, Will RG. *et al*. Iatrogenic Creutzfeldt–Jakob disease, final assessment. Emerg Infect Dis, 2012; 18:901-7.
51. Kincaid AE, Bartz JC. The nasal cavity is a route for prion infection in hamsters. J Virol, 2007; 81:4482-91.
52. Krüger D, Thomzig A, Lenz G, Kampf K, McBride P, Beekes M. *et al*. Faecal shedding, alimentary clearance and intestinal spread of prions in hamsters fed with scrapie. Vet Res, 2009; 40:4.
53. McCulloch L, Brown KL, Bradford BM, Hopkins J, Bailey M, Rajewsky K. *et al*. Follicular dendritic cell-specific prion protein (PrP) expression alone is sufficient to sustain prion infection in the spleen. PLoS Pathog, 2011; 7:e1002402.
54. Seelig DM, Mason GL, Telling GC, Hoover EA. Chronic wasting disease prion trafficking via the autonomic nervous system. Am J Pathol, 2011; 179:1319-28.
55. Urwin PJ, Mackenzie JM, Llewelyn CA, Will RG, Hewitt PE. Creutzfeldt-Jakob disease and blood transfusion: Updated results of the UK Transfusion Medicine Epidemiology Review Study. Vox Sang, 2016; 110:310-16.
56. Belay ED, Schonberger LB. The public health impact of prion diseases. Ann Rev Pub Health, 2005; 26:191-212.
57. Saunders SE, Bartelt-Hunt SL, Bartz JC. Occurrence, transmission, and zoonotic potential of chronic wasting disease. Emerging Infectious Diseases, 2012; 18:369-76.
58. Miller MW, Williams ES. Horizontal prion transmission in mule deer. Nature, 2003; 425:35-6.
59. Yuan Q, Eckland T, Telling G, Bartz J, Bartelt Hunt S. Mitigation of prion infectivity and conversion capacity by a simulated natural process—repeated cycles of drying and wetting. PLoS Pathog, 2015; 11:e1004638.
60. Johnson CJ, Bennett JP, Biro SM, Duque Velasquez JC, Rodriguez CM, Bessen RA, *et al*. Degradation of the disease-associated prion protein by a serine protease from lichens. PLoS One, 2011; 6:e19836.
61. Ding N, Neumann NF, Price LM, Braithwaite SL, Balachandran A, Belosevic M. *et al*. Ozone inactivation of infectious prions in rendering plant and municipal wastewaters. Sci Total Environ. 2014; 470(471):717-25.