Beside for intercellular route (cevc 2004, tang et

Beside SC, tight junction proteins (claudin, occluding and zonulaoccludins-1) have been implicated for providing barrier function to skin . Otherthan barrier like property of skin outside, there are many factors which affectthe delivery of the drug and they are discussed in the following section. FACTORS AFFECTING NANO BASEDTRANSDERMAL DRUG DELIVERYSYSTEM PARTICLE SIZE and ShapeThe nanodrugs transdermal delivery is affected by its size and shape which further decide physical steadinessand their cellular uptake (Escobar Chavez et al 2012). Nanoformulations can bedelivered concurrently using different means/routes owing to their particlesize and physicochemical properties (Borali 2010). Skin anatomical featuresonly allows free distribution of particles <5-7 nm size throughtranscellular route (Bouwstra and Ponec 2006, Johnson et al 1997), ? 36 nm forintercellular route (Cevc 2004, tang etal. 2001) and > 3-10 µm for transfollicular route.

Particles of smaller sizeare preferred since they make available larger surface area hence can have highdrug loading capacity. Attama et al (2007) reported that low particle size solid lipidnanodispersions (SLN) aremore stable and well accepted in vivo and active formulkation had high drugconcentration. Maestrelli et al (2009), who investigated ethosomes prepared by differenttechniques made similar conclusions and found that small unilamellar vesicles(SUVs) drug efficacy of benzocaine (BZC) was owing to its small size, highersurface area which led to more intimate contact with the epithelium for longerduration of time for therapeutic action.

Desaiet al. (2010) and Baroli (2010) concluded that lipophilic nanoparticles havehigh partition coefficient and drugs having molecular weight <600 Da

arebest suited for TDDS. Nanoparticles come in different shapes like spherical, ellipsoidal, triangular, needle shaped, cubic and prism like. They are notalways rigid (e.

g. lipid particles) and deformable. The shape as well asorientation of the nanoparticles greatly affects their aggregation, penetrationroute and diffusion coefficient (Baroli 2010).

Using newer methods ofnanomaterial synthesis, nanoparticles of preferred size and shape for TDDS canbe engineered. ZETA POTENTIALZetapotential is defines as the number of charges a particle has and particle sizedistribution and zeta potential of nanoformulations decides the dispersion steadiness of the non-aqueoussuspension. SIZE DISTRIBUTION Preparationmethods and conditions (like temperature, dispersing medium, stirring rate andviscosity of the organic and aqueous phases) affect the size distribution of nanoparticlesformed by different systems. Skin SURFACE PROPERTIESSurface properties of the skin like surface charge andpolarity are also key determinants for drug penetration profile in TDDS. Charges on the skin surface generally influencethe ionic interaction of drug molecules with cell membrane, route ofpenetration and diffusion rate in vivo. Surface charge of the cell membrane isdue to presence of negatively charged phosphatidyl choline and sulphatedproteoglycans. They are membrane anchored core proteins which areliked to glycosaminoglycan side chains (heparan, dermatan, keratan orchondrotine sulfates) that obtrude from the cell surface.

Due to this negativecharge in skin at neutral pH, positively charged nano formulations diffuseeffectively through skin. Hoeller et al.(2009) reported

effective permeation of drug though porcine skin usingphytosphingosine (PS) containing positive charged nanoemulsion than thenegatively charged ones. Generally negatively charged nanoparticlesare repelled by cellular membrane, however they are absorbed by non specificprocess of nanoparticle cluster formation at positive charged sites whichlead to neutralization followed by cellular uptake by the process ofendocytosis