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Molecular insights into shellac film coats from different aqueous shellac salt solutions and effect on disintegration of enteric-coated soft gelatin capsules

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ABSTRACT

The purpose of this investigation was to study the effect of using different salts of shellac on the disintegration properties of shellac-based enteric coatings. In the last two decades, shellac has been increasingly used as an aqueous solution for enteric coating purposes, with the ammonium salt being the form typically used. Little investigation has been performed on using other salts, and therefore, this was the focus of our work. Enteric coatings, based on different shellac salts (ammonium, sodium, potassium and composite ammonium–sodium), were applied onto soft gelatin capsules. Disintegration testing of the coated soft gelatin capsules showed that alkali metal salts promote faster disintegration than ammonium salts. In order to determine the causes behind these differences, the solubility, thermal and spectroscopic properties of films cast from the different salts were investigated. The results show that films cast from ammonium-based salts of shellac are, unlike those cast from alkali metal-based salts, water-insoluble. Spectroscopic evidence suggests that this might be due to partial salt dissociation resulting in loss of ammonium as ammonia and reduced degree of shellac ionization during drying. In addition, oxidation of shellac aldehyde groups of the ammonium-based shellac salts could also play a role. And possible higher extent of shellac hydrolysis during the preparation of alkali metal salts might also be a factor. Therefore, the nature of the shellac salt used in the preparation of shellac-based aqueous coating solutions is a significant formulation factor affecting product performance.

1. Introduction

Shellac is the refined form of lac a natural resin obtained from insects belonging to the *Kerria* genus, mainly *Kerria lacca* in India and *Kerria chinensis* in Thailand, which are parasitic on certain trees (Chen et al., 2011; Mukhopadhyay and Muthana, 1962). The insect forms the resin internally from the sap of the tree and then secretes it through its body surface. The accumulating resin forms thick encrustations on the twigs that are scrapped off and then subjected to a sequence of refining steps. The final refined lac product is called shellac (Buch et al., 2009; Jasti et al., 2009).

Chemically, shellac is a mixture of polyesters made up of sesquiterpenoid acids (the major one among them being the aldehyde-containing jalaric acid) esterified with hydroxy fatty acids (the major one among them being aleuritic acid) (Wang et al., 1999). The resin has two fractions: a soft fraction made up of single esters of a sesquiterpenoid acid and a hydroxy fatty acid, and a hard fraction in which the aforementioned single esters are polymerized by ester linkages (Wang et al., 1999). The chemical structure of shellac is illustrated in Fig. 1.

Shellac is insoluble in water but soluble in various solvents like methanol and ethanol (Bose et al., 1963). The presence of carboxyl groups means that it has the potential to be used as an enteric coating film former in pharmaceuticals. Indeed, shellac, applied in the form of an alcoholic solution, was commonly used in the past as an enteric coating material; however, its use declined due to stability issues associated with the esterification and polymerization of shellac within the film (Penning, 1996). But this problem can be overcome by the application of shellac as an aqueous system made by forming the water-soluble ammonium salt of shellac, where ionization of the carboxyl groups will hinder their ability to participate in esterification reactions (Penning, 1996).

Since the 1990s, the use of shellac has experienced a degree of resurgence due to the coatings obtained from the ammonium salt-based aqueous solutions of shellac exhibiting a superior degree of stability compared to those obtained from the traditional alcoholic

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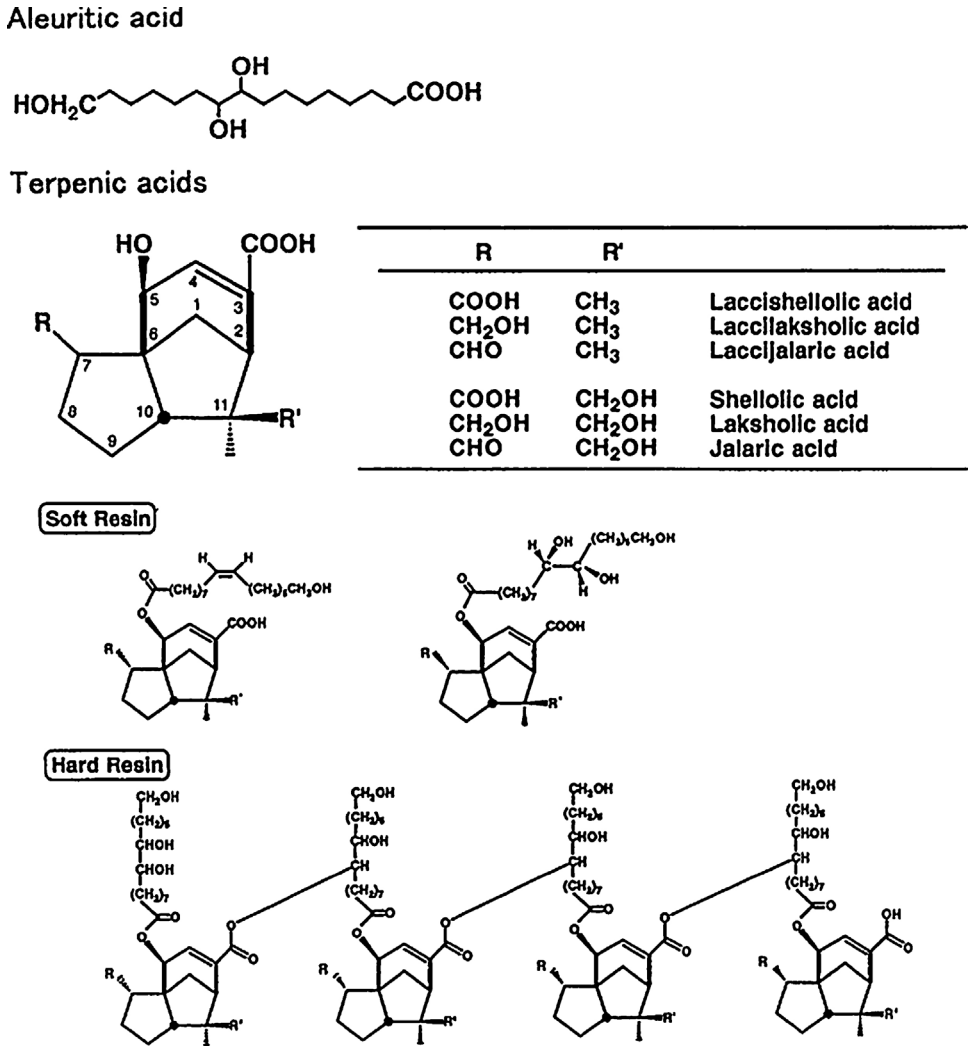

Fig. 1. Chemical structure of shellac constituents (Wang et al., 1999).

systems (Farag and Leopold, 2011). But failure to disintegrate in the proximal small intestine is still a potential problem facing shellac-coated dosage forms (Limmatvapirat et al., 2007), and research is needed to minimize this problem.

One possible approach to modify the disintegration properties of shellac-based enteric coatings is to employ different salts of shellac. However, research into using salts other than the ammonium salt has been limited. Some work was performed on the 2-amino-2-methyl-1-propanol (2-AMP) salt (Luangtana-anan et al., 2007; Limmatvapirat et al., 2007) where, for partially hydrolyzed shellac, films cast from a solution of this salt dissolved more readily, in pH 7.0 and 7.3 buffers, than films cast from an ammonium salt solution (Limmatvapirat et al., 2007). However, to the best of our knowledge, 2-amino-2-methyl-1-propanol is not approved as a direct food additive by the FDA or the EU, preventing its use in nutritional supplements. Moreover, the enteric properties were evaluated only for partially hydrolyzed shellac, and for free films instead of coated dosage forms. Osman, in his thesis, has also shown that pellets coated with a sodium shellac salt-based formulation exhibited a faster drug release than those coated with an ammonium salt-based formulation (Osman, 2012), but his dissolution experiments did not involve consecutive exposure of the same pellets to acid followed by near-neutral pH buffer, and so did not simulate the succession of pH conditions to which the dosage form will be exposed in the human gastro-intestinal (GI) tract.

Therefore, the focus of this work was to compare the disintegration properties of enteric coatings based on different shellac salts, and to attempt to explain the differences in these properties. Gloss and mechanical properties of these coatings were also studied. The compared salts were the ammonium salt, the sodium salt, the potassium salt and a composite ammonium–sodium salt made using equimolar proportions of ammonium and sodium ions. Salts of these ions can be prepared using their respective bicarbonates which are approved as direct food additives (FDA, 2014), and so can be used also in nutritional supplements, an area where shellac, owing to its natural origin, fits well into the product image (Pearnchob et al., 2004).

2. Materials and methods

2.1. Materials

Bysakhi-based HS 702 orange dewaxed shellac, refined by solvent extraction, was received as a gift from A.F. Suter (Witham, United Kingdom). Placebo size 4 oval soft gelatin capsules were received as a gift from Catalent Pharma Solutions (Eberbach, Germany). HPMC (Pharmacoat 606) was received as a gift from HARKE (Muelheim an der Ruhr, Germany). All the other materials used were of analytical grade.