Evaluation of *Stryphnodendron* sp. Release Using Natural Rubber Latex Membrane as Carrier

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**Abstract:** Natural rubber latex from *Hevea brasiliensis* has interesting characteristics related to this work such as: it is easy to manipulate, low cost, can stimulate the natural angiogenesis, is a biocompatible material and presents high mechanical resistance. The aim of this study was to develop a novel sustained delivery system for *Stryphnodendron* sp. based on Natural Rubber Latex (NRL) membranes and to study the *Stryphnodendron* sp. delivery system behavior. *Stryphnodendron* sp., commonly known as barbatimão, is extensively used in folk medicine for the treatment of diarrhoea, gynaecological problems and for healing wounds. The stem bark of this species is mentioned in the Brazilian Pharmacopoeia with a content of at least 20% of tannins. Previous studies showed significant cicatrizing properties, anti-inflammatory activity and gastric anti-ulcerogenic effects for the stem bark crude extract. One possible way to accelerate the tissue repair process, it was incorporated the *Stryphnodendron* sp. extract in NRL membranes. *Stryphnodendron* sp extract was incorporated into the NRL, by mixing it in solution for in vitro protein delivery experiments. Results show that the NRL membrane can release *Stryphnodendron* sp for up to 49.89% of its *Stryphnodendron* sp content for up 400 h. The kinetics of the extract release could be fitted with double exponential function, with two characteristic times of 0.78 and 133.22 h. In this study, we demonstrated that the induced angiogenesis provided by NRL membranes combined with a controlled release of extract is relevant for biomedical applications.

**Key words:** *Stryphnodendron* sp., biomaterials, natural rubber latex, drug delivery system, barbatimão

### INTRODUCTION

The controlled release of drugs/extracts can be efficient if a suitable encapsulation procedure is developed, which requires biocompatible materials to hold and release the drug/extracts. In this study, NRL membrane is used to deliver *Stryphnodendron* sp extract. Latex membrane from *Hevea brasiliensis* is an important inductor of wound healing, regeneration of organism. (Ereno et al., 2010; Sampaio et al., 2010; Herculano et al., 2011a; Ciacetti et al., 1994; Mendonça and Coutinho-Netto, 2009). In addition, the treatment of diabetic and phlebothrombosis ulcers with the biomembrane prepared from the natural latex showed the presence of a vascular growth factor in the latex (Balabanian et al., 2006; Mendonça and Coutinho-Netto, 2009; Ferreira et al., 2009; Frade et al., 2001; Mena et al., 2004). *Stryphnodendron* sp., commonly known as barbatimão, is extensively used in folk medicine for the treatment of diarrhoea, gynaecological problems and for healing wounds. The stem bark of this plant contains a considerable amount of tannin (10-37%) and prominent presence of several flavan-3-ols, proanthocyanidins and procorbinetimidas (Lopes et al., 2005; Lima et al., 1998; Holetz et al., 2005; Santos et al., 2002). The crude extract, in the form of decoction or infusion, is traditionally used by the local population for the treatment of leucorrhoea and diarrhoea, as well as an anti-inflammatory and healing agent (Di Mambro et al., 2005; Castro et al., 2009; Eurides et al., 1995). Some studies of the crude extract from the stem bark of *Stryphnodendron adstringens* have revealed significant anti-inflammatory activity and gastric anti-ulcerogenic effects. It has also been observed that a decoction of the stem bark of *Stryphnodendron* sp accelerates the healing of wounds and decreases inflammation (Minatel et al., 2010). One possible way to accelerate the tissue repair

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process, it was incorporated the *Strychnodendron* sp. extract in NRL. *Strychnodendron* sp. extract was incorporated into the NRL, by mixing it in solution for *in vitro* protein delivery experiments. NRL membranes have already been used to deliver drugs (Herculano et al., 2006, 2007, 2009, 2010).

In this study, we propose a novel release system based on the encapsulation of *Strychnodendron* sp. in NRL membrane for the sustained and controlled delivery of *Strychnodendron* sp. for future applications in medicine as wound healing. Results show that the NRL membrane can release *Strychnodendron* sp. for up to 400 h, which is relevant for biomedical applications.

MATERIALS AND METHODS

The NRL used in the present study was commercial high-ammonia natural rubber latex (ESALQ-USP, Pirassununga, Brazil) of about 60% dry rubber content (DRC), 4-5% weight of non-rubber constituents such as protein, lipids, carbohydrates and sugar and 35% of water (Hashim and Subramaniam, 1986; Yip et al., 1994; Yip and Sussman, 2000). After extraction, ammonia was used to keep the latex liquid. The deproteinization of natural rubber latex was performed by centrifugation at 8,000 g. The cream fraction after centrifugation was re-dispersed to make 60 wt.% of dry rubber content latex and was washed twice by centrifugation to prepare the deproteinized natural rubber latex and then reduce the cytotoxic protein content on NRL. *Strychnodendron* sp., commonly known as barbatimão were collected in March 2011 at Paranapanema Valley region, (Sao Paulo State, Brazil). The barks extract (20 g) was extracted by stirring in an Erlenmeyer at room temperature with acetone/water 7:3 (4×100 mL). These extract was evaporated under vacuum to 30% volume and filtered to remove fats and then freeze-dried. Extract of *Strychnodendron* sp. was incorporated by mixing 2 mL of natural rubber latex with 2 mL of extract solution (10 mg mL⁻¹). These membranes were prepared by pouring the latex+extract solution in a stainless steel plate with 5.00±0.05 cm diameter and 200±5.00 μm thick. Typically the membranes were left for 2 days to fully polymerize before use. For the study of the release of extract, latex membrane was placed in 200 mL of an aqueous solution, from which aliquots were collected during an interval ranging from 10 to 24,000 min. The extract released into the solution was monitored by measuring the UV-VIS spectra with a BEL ENGINEERING SF 200 ADV spectrophotometer, as *Strychnodendron* sp. extract has a maximum absorption at 297 nm.

RESULTS AND DISCUSSION

The goal of controlled-release delivery systems is to provide desirable delivery patterns so that predictable plasma drug/extract levels can be achieved, which requires the characterization of the basic pharmacodynamic and pharmacokinetic properties of a drug/extract. For *Strychnodendron* sp. studied here, it has been found that it absorbs at 297 nm. In Fig. 1 shows the absorbance intensity as a function of *Strychnodendron* sp. concentration in solution.

The sustained delivery system for *Strychnodendron* sp. has been successfully developed based on NRL. The release profile for *Strychnodendron* sp. in a NRL matrix in Fig. 2 shows that the first, fast step of burst release corresponded to the *Strychnodendron* sp. near or on the surface of the NRL membrane (Herculano et al., 2011b). The slower release process would be associated with *Strychnodendron* sp. diffusing slowly through the matrix. Results demonstrated that the NRL membrane can release *Strychnodendron* sp. for 15 days.

The experimental data in Fig. 2 were fitted using a bi-exponential function \( y(t) = y_1 + A_1 e^{-\delta_1 t} + A_2 e^{-\delta_2 t} \), where \( y(t) \) was the amount of *Strychnodendron* sp. in the NRL at a
Wang et al. (2005) prepared uniform-sized chitosan microspheres by membrane emulsification technique. Uniform chitosan microspheres were further used as a carrier of protein drug (BSA). They observed that BSA loading efficiency was highest when pH value was 8.09 and it decreased with an increase of the crosslinking degree.

Herculano et al. (2011b) proposed a drug release system based on NRL for the sustained and controlled delivery of metronidazole (MET). They concluded that the release time of MET in in vitro tests was very promising for the kinetics of release.

Our results indicate that with very simple changes in preparation of NRL membrane, we could control Stryphnodendron sp. release up to 15 days, according to Woo et al. (2001), Wang et al. (2005), Herculano et al. (2011b), Malcolm et al. (2004) and Langer and Folkman (1976) results, or in other words with a slow release rate.

**CONCLUSION**

We have prepared natural rubber latex membranes containing Stryphnodendron sp. as a model system for tissue regeneration. The method of preparation is reproducible and the natural rubber latex membrane is very stable. Results demonstrated that the NRL membrane can release Stryphnodendron sp. for 15 days, thus making them promising materials for protein/extract release in *in vivo* applications. We have observed that 44.89% of the initial Stryphnodendron sp. content inside NRL was released in 400 h. Our results indicate that NRL could be used in the future as an active membrane that could accelerate tissue healing.

**ACKNOWLEDGMENTS**

This work was supported by PROPe/UNESP and FAPESP (Processes: 2011/17411-8, 2011/06856-9).

**REFERENCES**


