

REFERENCES

- Aiba, S. (1986) Studies on chitosan: I. Determination of the degree of N-deacetylation of chitosan by ultraviolet spectrophotometry and gel permeation chromatography. *Int. J. Biol. Macromol.*, 8, 173-176.
- Akashi, M., Sakamoto, N., Suzuki, K. and Kishida, A. (1996) Synthesis and anticoagulant activity of sulfated glucoside-bearing polymer. *Bioconjugate Chem.*, 7, 393-395.
- Anaclerio, A., Ruggeri, A. and Poggi, A. (1980) *In vivo* and *in vitro* immunosuppressive effect of two batroxobin preparation in mice. *Thromb. Res.*, 18, 253-256.
- Andersson, L.O., Barrowcliffe, T.W., Holmer, E., Johnson, E.A. and Sims, GEC. (1976) Anticoagulant properties of heparin fractionated by chromatography on matrix-bound antithrombin III and by gel filtration. *Thromb. Res.*, 9, 575-583.
- Asakura, S., Hirata, H., Okasaki, H., Hashimoto-Gotoh, T. and Matsuda, M. (1990) Hydrophobic residues 382-386 of antithrombin III, Ala-Ala-Ala-Ser-Thr, serve as the epitope for an antibody which facilitates hydrolysis of the inhibitor by thrombin. *J. Biol. Chem.*, 265, 5135-5138.
- Asemissen, A.M., Nagorsen, D., Kelholz, U., Letsch, A. Schmittl, A., Thiel, E., et al. (2001) Flow cytometric determination of intracellular or secreted IFN- γ for the quantification of antigen reactive T cells. *J. Immunol. Methods*, 251, 101-108.

- Atha, D.H., Lormeau, J.C., Rosenberg, R.D. and Choay, J. (1985) Contribution of monosaccharide residues in heparin binding to antithrombin III. *Biochemistry*, 24, 6723-6729.
- Barclay, A.N., Brown, M.H., Law, S.K.A., McKnight, A.J., Tomlinson, M.G. and van der Merwe, P.A. (1997) *The Leukocyte Antigen FactsBook*, 2nd ed., San Diego, Academic Press, Inc.
- Beresford, C.H. and Owen, M.C. (1990) Antithrombin III. *Int. J. Biochem.*, 22, 121-128.
- Biagini, G., Bertani, A., Muzzarelli, R., Damadei, A., DiBenedetto, G., Belligolli, A., et al. (1991) Wound management with N-carboxybutyl chitosan. *Biomaterials*, 12, 281-286.
- Bienkowski, M.J. and Conrad, H.E. (1985) Structural characterization of the oligosaccharides formed by depolymerization of heparin with nitrous acid. *J. Biol. Chem.*, 260, 356-365.
- Bjork, I., Yinenjarvi, K., Olson, S.T. and Bock, P.E. (1992) Conversion of antithrombin from an inhibitor of thrombin to a substrate with reduced heparin affinity and enhanced conformational stability by binding of a tetradecapeptide corresponding to the P1 to P14 region of the putative reactive bond loop of the inhibitor. *J. Biol. Chem.*, 267, 1976-1982.
- Bochtler, M., Diitzel, L., and Groll, M. (1999) The proteasome. *Ann. Rev. Biophysic. Biomolec. Struc.*, 28, 295-317.
- Bode, V. and Franz, G. (1991) Physiological activity of new heparinoids derived from plant polysaccharides. *Arch. Pharm. (Weinheim)*, 324, 363-365.

- Bonifacino, J.S. and Weissman, A.M. (1998) Ubiquitin and the control of protein fate in the secretory and endocytic pathways. *Ann. Rev. Cell Devel. Biol.*, 14, 9-58.
- Bonilla, C.A. (1975) Defibrinating enzyme from Timber Rattlesnake (*Crotalus J. horridus*) venom: A potential agent for therapeutic defibrination. I. Purification and properties. *Thromb. Res.*, 6, 151-169.
- Bourin, M. and Lindahl, U. (1990) Functional role of the polysaccharide component of rabbit thrombomodulin proteoglycans. Effects on inactivation of thrombin by antithrombin. *Biochem. J.*, 270, 419-425.
- Bourin, M. and Lindahl, U. (1993) Glycosaminoglycans and the regulation of blood coagulation. *Biochem. J.*, 289, 313-330.
- Busch, C. (1984). In E.A Jaffe (Ed.), *Biology of endothelial cells* (pp. 178-88), The Hague : Martinus Nijhoff.
- Calard, R.E. and Gearing, A.J.H. (1994) *The Cytokine FactsBook*. London : Academic Press.
- Carrell, R.W., Christey, P.B. and Boswell, D.R. (1987) in M. Verstraete, J. Vermeylen, H.R. Lijnen and J. Arnout (Eds.) *Thrombosis and haemostasis* (pp. 1-15), Leuven : Leuven University Press.
- Caso, R., Lane, D.A., Thompson, E.A., Olds, R.J., Thein, S.L., Paquin, M., et al., (1991) Antithrombin Vicenza, Ala 384 to Pro (GCA to CCA) mutation, transforming the inhibitor into a substrate. *Br. J. Haematol.*, 77, 87-92.
- Castellino, F. (1997) Antigen presentation by MHC class II molecules: invariant chain function, protein trafficking, and the molecular basis of diverse determinant capture. *Hum. Immunol.*, 54, 159-169.

- Casu, B. (1985) Structure and biological activity of heparin. *Adv. Carbohydr. Chem. Biochem.*, 43, 51-134.
- Casu, B., Colombo, M., Compagnoni, T., Naggi, A., Pivari, E. and Torri, G. (1986) in R.A.A. Muzzarelli, C. Jeuniaux, and G.W. Gooday (Eds.) (pp. 309-310), *Chitin in nature and technology*. New York : Plenum Press.
- Chandy, T. and Sharma, P. (1990) Chitosan- as a biomaterial. *Biomater. Artif. Cells Artif. Org.*, 18, 1-24.
- Clark, E.A., Shu, G.L., Luscher, B., Draves, K.E., Banchereau, J., Ledbetter, J.A., *et al.* (1989) Activation of human B cells. Comparison of the signal transduced by IL-4 to four different competence signals. *J. Immunol.*, 143, 3873-3880.
- Colburn, P. and Buonassisi, V. (1982) Anticlotting activity of endothelial cell cultures and heparan sulfate proteoglycans. *Biochem. Biophys. Res. Commun.*, 104, 220-227.
- Coleman, R.W., Hirsh, J., Marder, V.J. and Salzman, E.W. (1987) *Hemostasis and thrombosis* 2nd edition, Philadelphia : J.B Lippincott.
- Coligan, J.E., Kruisbeek, A.M., Margulies, D.H., Shevach, E.M. and Strober, W. (1994) *Current protocols in immunology*, USA : John Wiley & Sons, Inc.
- Comper, W.D. (1981) Heparin (and related polysaccharides) : Structural and functional properties. Vol.7, New York: Gordon and Breach.
- Cushing, I.B., Davis, R.V., Kratochvil, E.J. and MaccorQuodale, W. (1954) The sulfation of chitin in chlorosulfonic acid and dichloromethane. *J. Am. Chem. Soc.*, 76, 4590-4591

- Dahlback, B. (1991) Protein S and C4b-binding protein : components involved in the regulation of the protein C anticoagulant system. *Thromb. Haemostasis.*, 66, 49-61.
- Dahlback, B. (1995) New molecular insights into the genetics of thrombophilia: resistance to activated protein C caused by Arg506 to Gln mutation in factor V as a pathogenic risk factor for venous thrombosis. *Thromb. Haemostasis*, 74, 139-148.
- Danielsson, A., Raub, E., Lindahl, U. and Björk, I. (1986) Role of ternary complexes in which binds both antithrombin and proteinase, in the acceleration of the reactions between antithrombin and thrombin or factor Xa. *J. Biol. Chem.*, 261, 15467-15473.
- Davie, E.W. and Ratnoff, O.D. (1964) Waterfall sequence for intrinsic blood clotting. *Science*, 145, 1310-1312.
- Doczi, J., Fishman, A. and King, J.A. (1953) Direct evidence of the influence of sulfamic acid linkages on the activity of heparin-like anticoagulants. *J. Am. Chem. Soc.*, 75, 1512-1513.
- Duarte, M.L., Ferreira, M.C., Marvão, M.R. and Rocha, J. (2001) Determination of the degree of acetylation of chitin materials by ^{13}C CP/MAS NMR spectroscopy. *Int. J. Biol. Macromol.*, 28, 359-363.
- Ehlers, M.R. and Daffe, M. (1998) Interactions between *Mycobacterium tuberculosis* and host cells: are mycobacterial sugars the key?. *Trends Microbiol.*, 6, 328-335.
- Errichetti, A.M., Holden, A. and Ansell, J. (1984) Management of oral anticoagulant therapy : Experience with an anticoagulation clinic. *Arch. Intern. Med.*, 144, 1966-1968.

- Esmon, C.T. (1989) The roles of protein C and thrombomodulin in the regulation of blood coagulation. *J. Biol. Chem.*, 264, 4743-4746.
- Farndale, R., Buttle, D.J., and Barret, A.J. (1986) Improved quantitative and discrimination of sulfated glycosaminoglycan by use of dimethylmethylene blue, *Biochem. Biophys. Acta.*, 883, 173-174.
- Fenton, II, J.W. (1986) Thrombin. *Ann. N.Y. Acad. Sci.*, 485, 5-15.
- Fitzpatrick, D.R. and Bielefeldt-Ohmann, H. (1999) transforming growth factor beta in infectious disease: always there for the host and the pathogen. *Trends Microbiol.*, 7, 232-236.
- Furie, B. and Furie, B.C. (1988) The molecular basis of blood coagulation. *Cell*, 33, 505-518.
- Furie, B. and Furie B.C. (1992) Molecular and cellular biology of blood coagulation. *N. Engl. J. Med.*, 326, 800-806.
- Gamzazade, A., Sklyar, A., Nasibov, S., Sushkov, I., Shashkov, A. and Knirel, Yu. (1997) Structural features of sulfated chitosans, *Carbohydrate Polymers*, 34, 113-116.
- Germain, R.M. and Margulies, D.H. (1993) The biochemistry and cell biology of antigen processing and presentation. *Annu. Rev. Immunol.*, 11, 403-450.
- Gerwitz, A. (1995) Megakaryocytopoiesis: the state of the art. *Thromb. Haemostasis*, 74, 204-209.
- Geiger, M., Heeb, M.J., Binder, B.R. and Griffin, J.H. (1988) Competition of activated protein C and urokinase for a heparin-dependent inhibitor. *FASEB J.*, 2, 2263-2267.
- Gordon, S. (1999) (Ed.) *Phagocytosis: the host* , vol. 5, Stamford, JAI Press Inc.

- Gregory, S., Zilber, M., Charron, D. and Gelin, C. (2000) Human CD1a molecule expressed on monocytes plays an accessory role in the superantigen-induced activation of T lymphocytes. *Hum. Immunol.*, 61, 193-201.
- Griffith, M.J., Noyes, C.M. and Church, F.C. (1985) Reactive site peptide structural similarity between heparin cofactor II and antithrombin III. *J. Biol. Chem.*, 260, 2218-2225.
- Grimm, E.A., Mazumder, A., Zhang, H.Z. and Rosenberg, S.A. (1982) Lymphokine-activated killer cell phenomenon: lysis of natural killer-resistant fresh solid tumor cells by interleukin-2 activated autologous human peripheral blood lymphocytes. *J. Exp. Med.*, 55, 1823-1841.
- Hackman, R.H. (1954) Chitin. I. Enzymatic degradation of chitin and chitin esters. *Austr. J. Biol. Sci.*, 7, 168-178.
- Hay, H.D. (1991) *Cell biology of extracellular matrix*, 2nd ed, New York : Plenum Press.
- Hayashi, K., Imoto, T. and Funatsu, M. (1968) Crystallization of the lysozyme-product complex. *J. Biochem.*, 63, 550-552.
- Hayes, E.R. (1986) U.S. Patent 4619995 (October).
- Heeb, M.J., Espana, F., Geiger, M., Collen, D., Stump, D.C. and Griffin, J.H. (1987) Immunological identity of heparin-dependent plasma and urinary protein C inhibitor and plasminogen activator inhibitor-3. *J. Biol. Chem.*, 262, 15813-15816.
- Heeb, M.J. and Griffin, J.H. (1988) Physiologic inhibition of human activated protein C by alpha 1-antitrypsin. *J. Biol. Chem.*, 263, 11613-11616.

- Heuck, C.C., Schiele, U., Hom, D., Fronda, D. and Tirz, E. (1985) The role of surface charge on the accelerating action of heparin on the antithrombin III-inhibited activity of alpha-thrombin. *J. Biol. Chem.*, 260, 4598-4603.
- Hirano, S., Ohe, Y., Ono, H. (1976) Selective N-acylation of chitosan. *Carbohydr. Res.*, 47, 315-320
- Hirano, S., Tanaka, Y., Hasegawa, M., Tobetto, K. and Nishioka, A. (1985) Effect of sulfated derivatives of chitosan on some blood coagulant factors. *Carbohydr. Res.*, 137, 205-215.
- Hirano, S., Hasegawa, M. and Kinugawa, J. (1991) ^{13}C -n.m.r. analysis of some sulphate derivatives of chitosan. *Int. J. Biol.*, 13, 316-317.
- Hirohata, S. and Lipsky, P.E. (1989) T cell regulation of human B cell proliferation and differentiation. Regulatory influences of CD45R⁺ and CD45R⁻ T4 cell subsets. *J. Immunol.*, 152, 2597-2607.
- Hirst, J. (1991) Heparin. *N. Engl. J. Med.*, 324, 1565-1560.
- Hirst J., Dalen, J.E., Deykin, D. and Poller, L. (1992) Oral anticoagulants: mechanism of action, clinical effectiveness and optimal therapeutic range. *Chest*, 102(suppl), 312S-326S.
- Holmer, E., Söderström, G. and Andersson, L.O (1979) Studies on the mechanism of the rate-enhancing effect of heparin on the thrombin-antithrombin III reaction. *Eur. J. Biochem.*, 93, 1-5.
- Holme, K.R. and Perlin, A.S. (1997) Chitosan N-sulfate. A water-soluble polyelectrolyte. *Carbohydr. Res.*, 302, 7-12.

- Horton, D. and Just, E.K. (1973) Preparation from chitin of (1-4)-2-amino-2-deoxy-beta-D-glucopyrauronan and its 2-sulfoamino analog having blood-anticoagulant properties. *Carbohydr. Res.*, 29, 173-179.
- Hortin, G.L., Tollefsen, D.M. and Benutto, B.M. (1989) Antithrombin activity of a peptide corresponding to residues 54-75 of heparin cofactor II. *J. Biol. Chem.*, 264, 13979-13982.
- Horton, D. and Usui, T. (1978) Sulfated glycosaminoglycans obtained by chemical modification of polysaccharides. in R.G. Schweiger (Ed.), *Carbohydrate Sulfates*. (pp. 95), Washington, : ACS Symposium Series 77.
- Hovingh, P., Piepkorn, M. and Linker, A. (1986) Biological implications of the structural, antithrombin affinity and anticoagulant activity relationships among vertebrate heparins and heparin sulohates. *Biochem. J.*, 237, 573-581.
- Hoylaerts, M., Owen, W.G. and Collen, D. (1984) Involvement of heparin chain length in the heparin-catalyzed inhibition of thrombin by antithrombin III. *J. Biol. Chem.*, 259, 5670-5677.
- Hurst, R.E., Poon, M.C. and Griffith, M.J. (1983) Structure-activity relationships of heparin. Independence of heparin charge density and antithrombin-binding domains in thrombin inhibition by antithrombin and heparin cofactor II. *J. Clin. Invest.*, 72, 1042-1045.
- Kaiser, B. and Hauptmann, J. (1994) Factor Xa inhibitors as novel antithrombotic agents: facts and perspectives. *Cardiovasc., Drug Rev.*, 12, 225-236.

- Kifune, K. (1987) medical remedies produced from chitin. in S. Hirano (Ed.) *The development and application of chitin and chitosan*, (pp.242-245), Tokyo : Indust. Tech. Assoc.
- Kjellén, L. and Lindahl, U. (1991) Heparin or heparan sulfate- what is the difference? *Thromb. Haemost.*, 12, 44-48.
- Kojima, T., Leone, C.W., Marchildon, G.A., Marcum, J.A. and Rosenberg, R.D. (1992) Isolation and characterization of heparan sulfate proteoglycans produced by cloned rat microvascular endothelial cells. *J. Biol. Chem.*, 267, 4859-4869.
- Kozak, R.W., Moody, C.E., Staiano-Coico, L. and Weksler, M.E. (1982) Lymphocyte transformation induced by autologous cells. XII. Quantitative and qualitative differences between human autologous and allogeneic reactive T lymphocytes. *J. Immunol.*, 128, 1723-1727.
- Kozbor, D., Trinchieri, G., Monos, D.S., Isobe, M., Russo, G., Haney, J.A., et al. (1989) Human TCR- γ^+/δ^+ , CD8⁺ T lymphocytes recognize tetanus toxoid in an MHC-restricted fashion. *J. Exp. Med.*, 169, 1847-1851.
- Kurita, K. (1995) in M. Yabuki (Ed.) *Chitin, chitosan handbooks*. (pp.228-255), Japan : Gihodo Press.
- Kusche, M., Backstrom, G., Riesenfeld, J., Petitou, M., Choay, J. and Lindahl, U. (1988) Biosynthesis of heparin. O-sulfation of the antithrombin-binding region. *J. Biol. Chem.*, 263, 15474-15484.
- Kusche, M. and Lindahl, U. (1990) Biosynthesis of heparin. O-sulfation of D-glucuronic acid units. *J. Biol. Chem.*, 265, 15403-15409.

- Kuziel, W.A. and Greene, W.C. (1991) in B.J. Thomson (Ed.) *The cytokine handbook*. (pp. 83-102), London : Academic Press.
- Lam, L.H., Silbert, J.E. and Rosenberg, R.D. (1976) The separation of active and inactive forms of heparin. *Biochim. Biophys. Res. Commun.*, 6, 570-577.
- Levy-Toledano, S., Gallet, C., Nadel, F., Bryckaert, M., Macloug, J. and Rosa, J.P. (1997) Phosphorylation and dephosphorylation mechanisms in platelet function: a tightly regulated balance. *Thromb. Haemostasis*, 78, 226-233.
- Lindblom, A., Bengtsson-Olivecrona, G. and Fransson, L-A. (1991) Domain structure of endothelial heparan sulfate. *Biochem. J.*, 279, 821-829.
- Lindahl, U. and Höök, M. (1978) Glycosaminoglycans and their binding to biological macromolecules. *Annu. Res. Biochem.*, 47, 385-417.
- Lindahl, U., Backstrom, G., Hook, M., Thunberg, L. and Fransson, L.A. (1979) Linker A: Structure of the antithrombin-binding site of heparin. *Proc. Natl. Acad. Sci. USA*, 76, 3198-3202.
- Linehan, M., Miller, E., Anglard, P., Merino, M. and Zbar, B. (1989) Improved detection of allele loss in renal cell carcinomas after removal of leukocytes by immune selection. *J. Nat. Cancer Inst.*, 81, 287-290.
- Linhardt, R.J., Ampofo, S.A., Fareed, J., Hoppensteadt, D., Mulliken, J.B. and Folkman, J. (1992) Isolation and characterization of human heparin. *Biochemistry*, 31, 12441-12445.
- Macfarlane, R.G. (1964) An enzyme cascade in the blood clotting mechanism and its functions as a biochemical amplifier. *Nature*, 202, 498-499.

- Maeda, M., Murakami, H., Ohta, H. and Tajima, M. (1992) Stimulation of IgM production in human-human hybridoma HB4C5 cells by chitosan. *Biosci. Biotech. Biochem.*, 56, 427-431.
- Maffei, A. (1997) MHC class I antigen processing pathways. *Hum. Immunol.*, 54, 891-103.
- Markwardt, F. and Nowak, G. (1980) The influence of drugs on disseminated intravascular coagulation (DIC). IV. Effects of the thrombin-like enzyme batroxobin on thrombin-induced DIC in rats. *Thromb. Res.*, 17, 103-111.
- Mbemba, E., Chams, V., Gluckman, J., Klatzmann, D. and Gattegno, L. (1992) Molecular interaction between HIV-1 major envelope glycoprotein and dextran sulfate. *Biochim. Biophys. Acta.*, 1138, 62-67.
- Medshitol, R. and Janeway, C.A. (1997) Innate immunity: impact on the adaptive immune response. *Curr. Opin. Immunol.*, 9, 4-9.
- Miale, J.B. (1977) *Laboratory medicine hematology*, 5th edition, St. Louis (MO) : C.V. Mosby Co.
- Mihai, D., Mocanu, G. and Carpov, A. (2001) Chemical reactions on polysaccharides I. Pullulan sulfation. *Eur. Polym. J.*, 37, 541-546.
- Minami, S., Okamoto, Y., Matsuhashi, A. and Shigemasa, Y. (1990) Fibroblast formation by regenerated chitin derivative. *The international symposium on chitin derivatives in life sciences*, Sapporo : Hokkaido University.
- Minami, S., Okatomo, Y., Tanioka, S. et al. (1993) Effects of chitosan on wound healing. in M. Yalpani (Ed.) *Carbohydrates and carbohydrate polymers*, (pp. 141-152), Chicago : ATL Press.

- Miyasaki, T. and Matsushima, Y. (1968) Amino hexoses: Preparation of partially O-carboxymethylated chitin and its component 3-O- and 6-O-carboxymethyl-2-deoxy-D-glucose and the corresponding alditols. *Bull. Chem. Soc. Japan*, 41, 2754-2757.
- Mottonen, J., Strand, A., Symersky, J., Sweet, R.M., Danley, D.E., Geoghegan, K.F., et al., (1992) Structural basis of latency in plasminogen activator inhibitor-1. *Nature* (London), 355, 270-273.
- Mourey, L., Samama, J.P., Delarue, M., Choay, J., Lormeau, J.C., Petitou, M. and Moras, O. (1990) Antithrombin III: structural and functional aspects. *Biochimie*, 72, 599-608.
- Mori, T., Irie, Y., Nishimura, S-I., Tokura, S., Matsuura, M. (1997) Endothelial cell responses to chitin and its derivatives. *J. Biomed. Mater. Res.*, 43, 469-472.
- Mori, T., Okumura, M., Matsuura, M., Ueno, K., Tokura, S., Okatomo, Y., et al. (1997) Effects of chitin and its derivatives on the proliferation and cytokine production of fibroblasts *in vitro*. *Biomaterials*, 18, 947-951.
- Mosser, D.M. and Karp, C.L. (1999) Receptor mediated subversion of macrophage cytokine production by intracellular pathogens. *Curr. Opin. Immunol.*, 11, 406-411.
- Murata, J., Saiki, I., Nishimura, S-I., Nishi, N., Tokura, S. and Azuma, I. (1989) Inhibitory effect of chitin heparinoids on the lung metastasis of B16-BL6 melanoma. *Jpn. J. Cancer Res.*, 80, 866-872.
- Muzzarelli, R.A.A. (1973) *Natural chelating polymers*, (pp. 83-227), New York : Pergamon Press.
- Muzzarelli, R.A.A. (1977) *Chitin*. Oxford: Pergamon.

- Muzzarelli, R.A.A. (1981) Italian Patent 22780A/81 (July, 7).
- Muzzarelli, R.A.A., Tanfani, F., Emanuelli, M., Pace, D.P., Chiurazzi, E. and Piani, M. (1984) Sulfated N-(carboxymethyl)chitosans. *Carbohydr. Res.*, 126, 225-231.
- Muzzarelli, R.A.A. (1985) in G.O. Aspinall (Ed.) *The polysaccharides*, Vol 3 (pp. 417-450), New York : Academic Press.
- Muzzarelli, R.A.A., Jeuniaux, C. and Gooday, G.W. (1986). *Chitin in nature and technology*. New York : Plenum.
- Muzzarelli, R., Baldassarre, V., Conti, F., et al. (1988) Biological activity of chitosan: ultrastructure study. *Biomaterials*, 9, 247-252.
- Nagasawa, K., Harada, H., Hayashi, S. and Misawa, T. (1972) Sulfation of dextran with piperidine-N-sulfonic acid, *Carbohydr. Res.*, 21, 420-426.
- Nagasawa, K. and Uchiyama, H. (1984) Anticoagulant properties of heparin preparation from different animal sources with equivalent high affinity for antithrombin III. *J. Biol. Chem.*, 95, 619-626.
- Nakasawa, T., Nakasawa, N., Ambrus, J.L. Jr. and Fauci, A.S. (1988) Differential effects of interleukin 2 vs B cell growth factor on human B cells. *J. Immunol.*, 140, 465-469.
- Naggi, A.M., Torri, G., Compagnoni, T. and Casu, B. (1986) Synthesis and physico-chemical properties of the polyampholyte chitosan 6-sulfate. In R.A.A. Muzzarelli, C. Jeuniaux and G.W. Gooday (Eds.), *Chitin in nature and technology* (pp. 371), New York : Plenum Press.
- Nishimura, K., Nishimura, S., Nishi, N., Saiki, I., Tokura, S. and Azuma, I. (1984) Immunological activity of chitin and its derivatives. *Vaccine*, 2, 93-99.

- Nishimura, K., Nishimura, S., Nishi, N., Numata, F., Tone, Y., Tokura, S., *et al.* (1985) Adjuvant activity of chitin derivatives in mice and guinea pig. *Vaccine*, 3, 379-384.
- Nishimura, K., Ishihara, C., Ukei, S., Tokura, S. and Azuma, I. (1986a) Stimulation of cytokine production in mice using deacetylated chitin. *Vaccine*, 4, 151-156.
- Nishimura, K., Nishimura, S., Seo, H., Nishi, N., Tokura, S. and Azuma, I. (1986b) Macrophage activation with multi-porous beads prepared from partially deacetylated chitin. *J. Biomed. Mater. Res.*, 20, 1359-1372.
- Nishimura, K., Nishimura, S., Seo, H., Nishi, N., Tokura, S. and Azuma, I. (1987) Effect of multiporous microspheres derived from chitin and partially deacetylated chitin on the activation of mouse peritoneal macrophages. *Vaccine*, 5, 136-140.
- Nishimura, S., Ikeuchi, Y. and Tokura, S. (1984) The adsorption of bovine blood proteins onto the surface of O-(carboxymethyl)chitin. *Carbohydr. Res.*, 134, 305-312.
- Nishimura, S., Nishi, N., Tokura, S., Nishimura, K. and Azuma, I. (1986a) Bioactive chitin derivatives. Activation of mouse peritoneal macrophages by O-(carboxymethyl)chitin. *Carbohydr. Res.*, 146, 251-258.
- Nishimura, S., Nishi, N., Tokura, S., Okie, W. and Somorin, O. (1986b) Inhibition of the hydrolytic activity of thrombin by chitin heparinoids. *Carbohydr. Res.*, 156, 286-292.
- Nishimura, S-I. and Tokura, S. (1986) Preparation and antithrombogenic activities of heparinoid from 6-O-(carboxymethyl)chitin. *Int. J. Macromol.*, 9, 225-232.

- Nishimura S-I., Kai, H., Shinada, K., Yoshida, T., Tokura, S., Kurita, K, *et al.* (1998) Regioselective syntheses of sulfated polysaccharides : specific anti-HIV-1 activity of novel chitin sulfates. *Carbohydr. Res.*, 306, 427-433.
- Noguchi, J., Wada, O., Seo, H., Tokura, S. and Nishi, N. (1973) Chitin and chitin-cellulose fibers. *Kobunshi Kagaku*, 30, 320-326.
- Nud' ga, L.A., Prisko, E.A. and Danilov, S.N. (1973) O-alkylation of chitosan. *Zhur. Obs. Khim.*, 43, 2752-2756.
- Ofosu, F.A., Modi G.J., Blajchman, M.A. and Buchanan, M.R. (1987) Increased sulfation improves the anticoagulant activities of heparan sulfate and dermatan sulfate. *Biochem. J.*, 248, 889-896.
- Okimasu, S. (1958) Studies of chitin from the standpoint of polymer chemistry : relation of the effective charges of glycolchitosan and its N-methyl derivative on interaction with negative colloids. *Nippon Nogei Kagaku*, 32, 298-302.
- Okatomo, Y., Minami, S. and matsuhashi, A. (1991) Application of chitin and chitosan in small animals. in C.J.. Brine, P.A. Sandford, J.P. Zikakis (Eds.) *Advances in chitin and chitosan.* (pp. 70-78), New York : Elsevier.
- Okatomo, Y., Minami, S., Matsuhashi, A., *et al.* (1993) Application of polymeric N-acetyl-D glucosamine (chitin) to veterinary practice. *J. Vet. Med. Sci.*, 55, 743-747.
- Olson, S.T. (1985) Heparin and ionic strength-dependent conversion of antithrombin III from an inhibitor to a substrate of alpha-thrombin. *J Biol. Chem.*, 260, 10153-10160.
- Olson, S.T. and Bjork, I. (1992) in L.J. Beriner (Ed.) *Thrombin: structure and function.* New York : Plenum.

- Otterlei, M., Varum, K.M., Ryan, L. and Espevik, T. (1994) Characterization of binding and TNF- α -inducing ability of chitosans on monocytes: the involvement of CD14. *Vaccine*, 12, 825-832.
- Parker, K.A. and Tollefsen, D.W. (1985) The protease specificity of heparin cofactor II. Inhibition of thrombin generated during coagulation. *J. Biol. Chem.*, 260, 3501-3505.
- Parisher, E. and Lombardi, D. (1989) *Chitin Source book*. New York : John Wiley & Sons.
- Pasi, K. J. (1999). Hemostasis: Components and Process. in D.J. Perry and K.J. Pasi (Eds.), *Hemostasis and thrombosis protocols* (pp. 5), New Jersey : Humana Press.
- Pavao, M.S.G. and Mauro, P.A.S. (1995) A unique dermatan sulfate-like glycosaminoglycan from ascidian. Its structure and the effect of its unusual sulfation pattern on anticoagulant. *J. Biol. Chem.*, 270, 31027-31036.
- Pejler, G., Daneilsson, A., Bjork, I., Lindahl, U., Nader, H.B. and Dietrich, C.P. (1987) Structure and antithrombin-binding properties of heparin isolated from the clams *Anomalocardia brasiliana* and *Tivela mactroides*. *J. Biol. Chem.*, 262, 11413-11421.
- Perry, D.J. (1994) Antithrombin and its inherited deficiencies. *Blood Rev.*, 8, 35-37.
- Peterson, C.B. and Blackburn, M.N (1987) Antithrombin conformation and the catalytic role of heparin. II Is the heparin-induced conformational change in antithrombin required for rapid inactivation of thrombin?. *J. Biol. Chem.*, 262, 7559-7566.
- Piron, E. and Domard, A. (1997) Interaction between chitosan and uranyl ions. Part I. Role of physicochemical parameters. *Int. J. Biol. Macromol.*, 21, 327-335.

- Pomerantz, M.W. and Owen, W.G. (1978) A catalytic role of heparin. Evidence for a ternary complex of heparin cofactor thrombin and heparin. *Biochim., Biophys. Acta.*, 535, 66-77.
- Porcelli, S.A., Segelke, B.W., Sugita, M., Wilson, I.A. and Brenner, M.B. (1998) The CD1 family of lipid antigen-presenting molecules. *Immunol. Today*, 19, 362-268.
- Porcelli, S.A. and Modinlin, R.L. (1999) The CD1 system: antigen-presenting molecules for T cell recognition of lipids glycolipids. *Annu. Rev. Immunol.*, 17, 297-329.
- Pratt, C.W. and Church, F.C. (1992) Heparin binding to protein C inhibitor. *J. Biol. Chem.*, 267, 8789-8794.
- Pretolani, M. (1999) Interleukin-10: an anti-inflammatory cytokine with therapeutic potential. *Clin. Exp. Allergy*, 29, 1164-1171.
- Prochazkova, S., Vårum, K.M. and Østgaard, K. (1999) Quantitative determination of chitosans by ninhydrin, *Carbohydrate Polymers.*, 38, 115-122.
- Ragg, H. and Preibisch, G. (1988) Structure and expression of the gene coding for the humanserpin hLS2. *J. Biol. Chem.*, 263, 12129-12134.
- Rapaport, S.I. and Rao, L.V. (1995) The tissue factor pathway: how it has become a "prima ballerina". *Thromb. Haemostasis*, 74, 7-17.
- Rayner, A.A., Grimm, E.A., Lotze, M.T., Chu, E.W. and Rosenberg, S.A. (1985) Lymphokine-activated killer (LAK) cells: analysis of factors relevant to the immunotherapy of human cancer. *Cancer*, 55, 1327-1333.
- Roberts, G.A.F. and Domszy, J.G. (1982) Determination of the viscometric constants for chitosan. *Int. J. Biol. Macromol.*, 4, 374-377.
- Roberts, G.A.F. (1992) *Chitin chemistry*. London, Macmillan Press.

- Rodén, L. (1980) in W.J. Lennarz (Ed.) *The Biochemistry of glycoproteins and proteoglycans* (pp. 267-371), New York : Plenum.
- Rider, C.C., Coombe, D., Harrop, H., Hounsell, E., Bauer, C., Feeny, J., et al. (1994) Anti HIV-1 activity of chemically modified heparins : correlation between binding to the V3 loop of gp 120 and inhibition of cellular HIV-1 infection *in vitro*. *Biochemistry*, 33, 6974-6980.
- Rodén, L. (1989). In land D.A. and Lindahl U., (Eds). *Heparin: Chemical and biological properties, Clinical applications*. (pp.1-23), London : Edward Arnold.
- Rogers, S.J., Pratt, C.W., Whinna, H.C. and Church, F.C. (1992) Role of thrombin exosites in inhibition by heparin cofactor II. *J. Biol. Chem.*, 267, 3613-3617.
- Rosenberg, R.D. and Damus, P.S. (1973) The purification and mechanism of action of human antithrombin-heparin cofactor. *J. Biol. Chem.*, 248, 6490-6505.
- Rosenberg, R.D. and Lam, L.H. (1979) Correlation between structures and function of heparin. *Proc. Natl. Acad. Sci. USA.*, 76, 1218-1222.
- Rosenberg, S.A. (1986) Adoptive immunotherapy of cancer using lymphokine-activated killer cells and recombinant interleukin-2. in V.T. DeVita, Jr., S. Hellman, and S.A. Rosenberg (Eds.) *Important advances in oncology* (pp.55-91), Philadelphia, J.B. Lippincott.
- Roy K, Mao H-O, Huang S-K, Leong KW. (1999) Oral gene delivery with chitosan-DNA nanoparticles generates immunologic protection in a murine model of peanut allergy. *Nat. Med.*, 5, 387-391.

- Rydyard, P.M., Whelan, A. and Fanger, M.W. (2000) Overview of the immune system. In B.D. Hames (Ed.) *Instant Notes in Immunology* (pp. 5-8), United Kingdom, Springer.
- Salzman, E.W., Rosenberg, R.D., Smith, M.H., Lindon, J.N. and Favreau, L. (1980) Effect of heparin and heparin fractions on platelet aggregations. *J. Clin. Invest.*, 65, 64-73.
- Samama, M.M., Walenga, J.M., Kaiser, B. and Fareed, J. (1997) Specific factor Xa inhibitors. In Verstraete, M., Fuster, V. and Topol, E. (Eds.) *Cardiovascular thrombosis: Thrombocardiology* (pp. 173-188), Brussels : Lippincott-Raven.
- Seldin, D.C., Seno, N., Austen, K.F. and Stevens, R.L. (1984) Analysis of polysulfated chondroitin disaccharides by high-performance liquid chromatography. *Anal. Biochem.*, 141, 291-300.
- Selvarangan, R., Goluszko, P., Popov, V., Singhal, J., Pham, T., Lublin, D.M. et al., (2000) Role of decay-accelerating factor domains and anchorage in internalization of Dr-fimbriated *Escherichia coli*. *Infect. Immun.*, 68, 1391-1399.
- Senju, R. and Okimasu, S. (1950) Chitin: Glycolation of chitin and the chemical structure of glycolchitin. *J. Agr. Chem. Soc. Japan*, 23, 432-437.
- Shalaby, M.R., Espevik, T., Rice, G.C., Ammann, M.A., Figari, I.S., Ranges, G.E., et al. (1988) The involvement of human tumor necrosis factors- α and - β in the mixed lymphocyte reaction. *J. Immunol.*, 141, 499-503.
- Shen Hen, T.M. and Wolfrom, M.L. (1959) The sulfonation of chitosan. *J. Am. Chem. Soc.*, 81, 1764-1766.

- Shibata Y, Foster LA, Metzger WJ, Myrvik QN. (1997) Alveolar macrophage priming by intravenous administration of chitin particles, polymers of N-acetyl-D-glucosamine, in mice. *Infection and Immunity*, 65, 1734-1741.
- Shively, J.E. and Conrad, H.E. (1976) Isotopic procedures in the structural analysis of heparin cofactor. *Biochemistry*, 15, 3932-3942.
- Shigemasa, Y., Matsuura, H., Sashiwa, H. and Saimoto, H. (1996) Evaluation of different absorbance ratios from infrared spectroscopy for analyzing the degree of deacetylation in chitin. *Int. J. Biol. Macromol.*, 18, 237-242.
- Shigemasa, Y., Morimoto, M., Saimoto, H., Okamoto, Y. and Minami, S. (1998) *Applications of chitin and chitosan for biomaterials*. Proceedings of the 3rd Asia-Pacific Chitin and Chitosan Symposium, (pp. 47-54) : Taiwan.
- Shore, J.D., Olson, S.T., Craig, P.A., Choay, J. and Björk, I. (1989) Kinetics of heparin action. *Ann. N.Y. Acad. Sci.*, 556, 75-80.
- Skriver, K., Wikoff, W.R., Patston, P.A., Tausk, F., Schapira, M., Kaplan, A.P. and Bock, S.C. (1991) Substrate properties of C1 inhibitor Ma (alanine 434---glutamic acid). Genetic and structural evidence suggesting that the P12-region contains critical determinants of serine protease inhibitor/substrate status. *J Biol. Chem.*, 266, 9216-9221.
- Smith, K.A. (1984) Interleukin 2. *Annu. Rev. Immunol.*, 2, 319-333.
- Smith, K.A. (1988) Interleukin-2: inception, impact, and implications. *Science*, 240, 1169-1176.

- Sosa, M.A., Fazely, F., Koch, J., Vercellotti, S. and Ruprecht, R. (1991) N-carboxymethylchitosan-N,O-sulfate as an anti-HIV-1 agent. *Biochim. Biophys. Res. Commun.*, 174, 489-496.
- Stein, P.E., Leslie, A.G.W., Finch, J.T., Tutnell, W.G., McLaughlin, P.J. and Carrel, R.W. (1990) Crystal structure of ovalbumin as a model for the reactive centre of serpins. *Nature (London)*, 347, 99-102.
- Stump, D.C., Thienpont, M. and Collen, D. (1986) Purification and characterization of a novel inhibitor of urokinase from human urine. Quantitation and preliminary characterization in plasma. *J. Biol. Chem.*, 261, 12759-12766.
- Suzuki, K., Nishioka, J., Kusumoto, H. and Hashimoto, S. (1984) Mechanism of inhibition of activated protein C by protein C inhibitor. *J. Biochem.*, (Tokyo), 95, 187-195.
- Suzuki, K. (1985) in I. Witt (Ed.) Protein C, biological and medical aspects, (pp. 43-58), New York : Walter de Gruyter, Berlin.
- Suzuki, K., Deyashiki, Y., Nishioka, J., Kurashi, K., Akira, M., Yamamoto, S., et al., (1987) Characterization of a cDNA for human protein C inhibitor. A new member of the plasma serine protease inhibitor superfamily. *J. Biol. Chem.*, 262, 611-616.
- Tan, S.C., Knor, E., Tan, T.K. and Wong, S.M. (1998) The degree of deacetylation of chitosan : advocating the first derivative UV-spectrophotometry method of determination. *Talanta*, 45, 713-719.
- Teien, A.N., Lie, M. and Abildgaard, U. (1976) Assay of heparin in plasma using a chromogenic substrate. *Thromb. Res.*, 8, 413-416.
- Teien, A.N. and Lie, M. (1977) Evaluation of an amidolytic heparin assay method: increased sensitivity by adding antithrombin III. *Thromb. Res.*, 10, 399-410.

- Thomson, A. (1998) *The cytokine handbook* 3rd edition. San diego, Academic Press Inc.
- Tokura, S., Nishi, N., Somorin, O. and Tsutsumi, A. (1983) Studies on Chitin VIII: Some properties of water soluble chitin derivatives. *Polym. J.*, 15, 485-489.
- Tokura, S., Hasegawa, O., Nishimura, S-I., Nishi, N. and Takatori, T. (1987) Induction of methamphetamine-specific antibody using biodegradable carboxymethyl-chitin. *Anal. Biochem.*, 161, 117-122.
- Tokura, S., Baba, S., Uraki, Y., Miura, Y., Nishi, N. and Hasegawa, O. (1990) Carboxymethyl chitin as a drug carrier. *Carbohydr. Polym.*, 13, 273-283.
- Tokura, S. and Tamura, H. (1998) *Chitin and its derivatives as biomedical materials*. Proceeding of the 3rd Asia-Pacific chitin and chitosan symposium, (pp. 55-71), Taiwan.
- Tollefsen, D.M., Petska, C.A., Monafu, W.J. (1983) Activation of heparin cofactor II by dermatan sulfate. *J. Biol. Chem.*, 258, 6713-6716.
- Tollefsen, D.M., Sugimori, T. and Maimone, M.M. (1990) Effect of low molecular weight heparin preparations on the inhibition of thrombin by heparin cofactor II. *Semin. Thromb. Haemostasis*, 16, 66-70.
- Tosato, G., Blaese, R.M. and Yarchoan, R. (1985) relationship between immunoglobulin production and immortalization by Epstein Barr virus. *J. Immunol.*, 135, 959-964.
- Travis, J. and Salveson, G.S. (1983) Human plasma proteinase inhibitors. *Annu. Rev. Biochem*, 52, 655-709.
- Trujillo, R. (1968) Preparation of carboxymethyl chitin. *Carbohydr. Res.*, 7, 483-485.

- Turner, M., Schweighoffer, E., Colucci, F., Disanto, J.P. and Tybulewicz, V.L. (2000) Tyrosine kinase SYK: essential function for immunoreceptor signaling. *Immunol. Today*, 21, 148-154.
- Uchida, Y. and Izume, M. (1989) in T. Anthonson and P. Sanford (Eds.) *Chitin and chitosan*. (pp.373-382), London : Elsevier Applied Science.
- Uchima, T., Imanishi, K., Saito, S., Araake, M., Yan, X.J., Fujikawa, H., *et al.* (1989) Activation of human T cells by toxic shock syndrome toxin-1: The toxin-binding structures expressed on human lymphoid cells acting as accessory cells are HLA class II molecules. *Eur. J. Immunol.*, 19, 1803-1809.
- Ulanova, M., Tarkowski, A., Hahn-Zoric, M. and Hanson, L.A. (1999) Participation of CD1 molecules in the presentation of bacterial protein antigen humans. *Scand. J. Immunol.*, 50, 387-393.
- Underhill, D.M., Ozinsky, A., Hajjar, A.M., Stevens, A., Wilson, C.V., Bassetti, M. and Aderem, A. (1999) The Toll-like receptor 2 is recruited to macrophage phagosome and discriminates between pathogens. *Nature*, 401, 811-815.
- Van Deerlin, V.M.D. and Tollefsen, D.M. (1991) The N-terminal acidic domain of heparin cofactor II mediates the inhibition of α -thrombin in the presence of glycosaminoglycans. *J. Biol. Chem.*, 266, 20223-20231.
- von Asmuth, E.J., Dentener, M.A., Bazil, V., Bouma, M.G., Leeuwenberg, J.F. and Buurman, W.A. (1993) Anti-CD14 antibodies reduce responses of cultured human endothelial cells to endotoxin. *Immunology*, 80, 78-83.
- Warner, D.T. and Coleman, L.L. (1958) Selective sulfonation of amino groups in amino alcohol. *J. Org. Chem.*, 23, 1133-1135.

- Whishtler, R.J. and Kosik, M. (1971) Anticoagulant activity of oxidized and O-sulfated chitosan. *Arch. Biochem. Biophys.*, 142, 106-110.
- White, J.G. (1994) Anatomy and structural organization of the platelet. In R.W. Coleman et al.(Eds.), *Hemostasis and thrombosis: Basic principles and clinical practice*, 3rd edition, Philadelphia : J.B. Lippencott Co.
- Whitnack, E., Bisno, A.L., Beachey, E.H. (1981) Hyarulonate capsule prevents attachment of a group A Streptococci to mouse peritoneal macrophages. *Infect. Immun.* 31, 958-991.
- Williams, W.T., Beutler, E., Erslev, A.J., Rundles, R.W. (1977) *Hematology*, 2nd edition, New York : McGraw-Hill.
- Wintrobe, M.M., Lee, G.R., Boggs, D.R., Bitchell, J.C., Foerster, J., et al. (1981) *Clinical hematology*, 8th edition, Philadelphia : Lea&Febiger.
- Wolfrom, M.L., Shen, T.M. and Summners, C.G. (1953) Sulfated nitrogenous polysaccharides and their anticoagulant activity. *J. Am. Chem. Soc.*, 75, 1519-1523.
- Wolfrom, M.L. and Shen Han, T.M. (1959) The sulfonation of chitosan. *J. Am. Chem. Soc.*, 81, 1764-1766.
- Yalpani, M., Johson, F. and Robinson, L.E. (1990) Antimicrobial activity of some chitosan derivatives. In C.J. Brine, P.A. Sandford, J.P.Zikakis (Eds.) *Advances in chitin and chitosan*, (pp. 541-548), New York : Elsevier.
- Yalpani, M., Johnson, F. and Robinson, LE. (1992) *Chitin and chitosan: Sources, Chemistry, Biochemistry, Physical Properties and Applications*. Amsterdam : Elsevier.

- Yin, E.T. and Wessler, S. (1970) Heparin-accelerated inhibition of activated factor X by its plasma inhibitor. *Biochim. Biophys. Acta*, 201, 387-390.
- Yoshida, T., Hatanaka, K., Uryu, T., Kaneko, Y., Suzuki, E., Miyano, H., *et al.* (1990) Synthesis and structural analysis of curdlan sulfate with a potent inhibitory effect in vitro of AIDS virus infection. *Macromol*, 23, 3717-3722.
- Yoshikawa, T., Murakami, M. and Furukawa, Y. (1983) The effect of defibrinogenation with batroxobin on endotoxin-induced disseminated intravascular coagulation in rats. *Thromb. Res.*, 31, 729-735.