

UE Projet tuteuré et bibliographie

Objectifs de l'UE : Réaliser une recherche bibliographique

Travailler en équipe – Gérer un projet

Réaliser un rapport et une présentation orale

Résultats d'apprentissage de la gestion de projet et du travail en équipe

Elaborer un projet

Prendre des décisions au sein de l'équipe

Partager les informations

Créer une dynamique d'équipe

Résultats d'apprentissage de la recherche bibliographique

Réaliser une recherche bibliographique à l'écrit

Évaluer la pertinence des ressources par rapport à l'environnement de recherche et à la problématique

Prendre du recul et avoir un regard critique sur le contenu des ressources

Sandrine Huclier : Sandrine.huclier@univ-nantes.fr

Frise chronologique – déroulé projet tuteuré

Semaine 37

1^{ère} séance : présentation générale du module, répartition des projets tuteurés

Semaine 38 : séance à la BU sur utilisation des outils Nantilus et Zotero
-séance sur référencement biblio

Semaine 40
2/10 : Construction du diagramme de Gantt du projet – version 1 début de projet

Semaine 45
9/11 : Dépôt CR réunions du groupe

En rouge : les LIVRABLES

Semaine 7

14/02
Remise du rapport final incluant tous les Gantt, et tous les CR de réunions de groupe + avec tuteur

SEPTEMBRE

OCTOBRE

NOVEMBRE

DECEMBRE

JANVIER

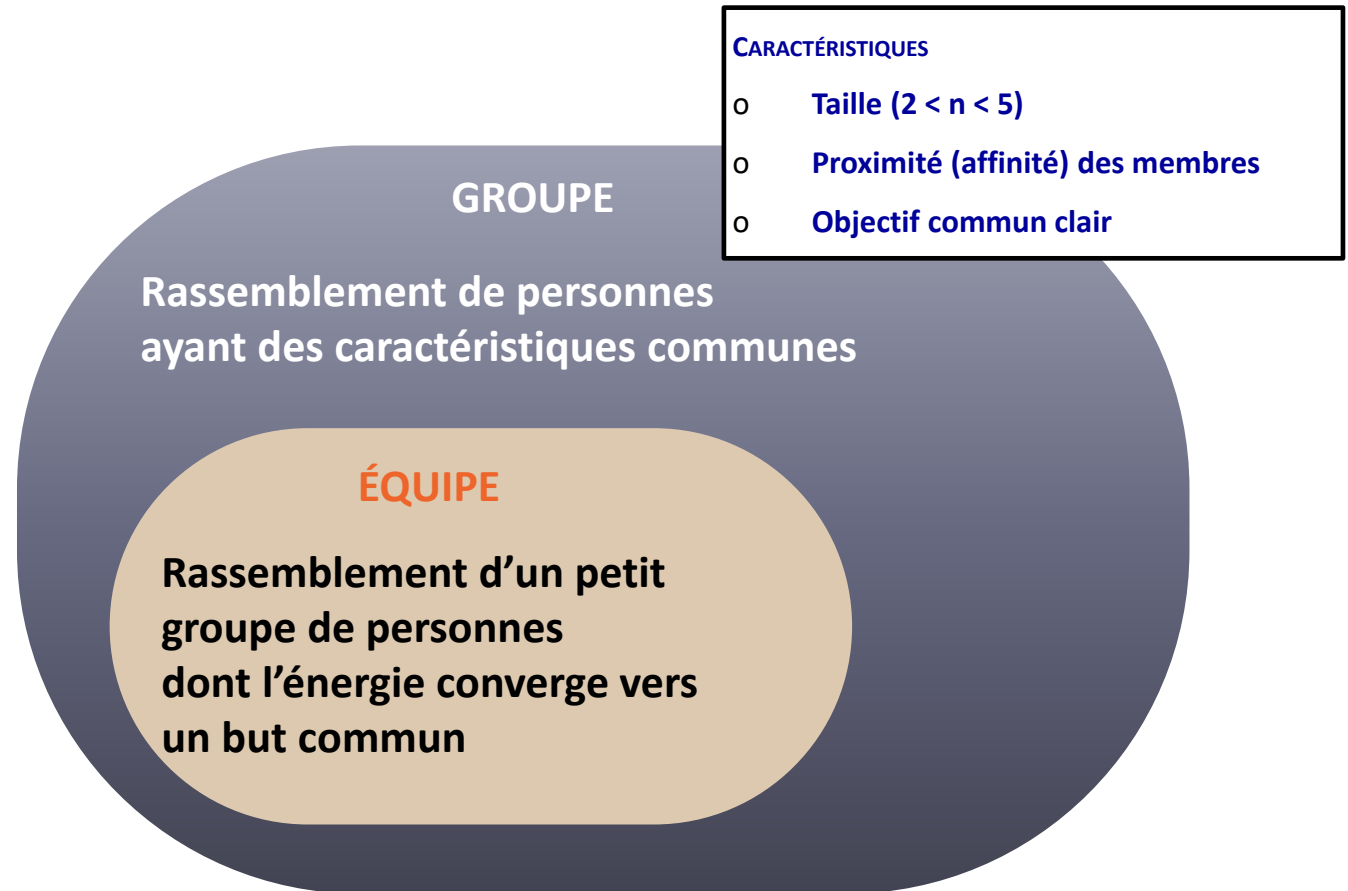
FEVRIER

Semaine 39
--visionner le tuto Gantt project

Semaine 50
14/12
- Mise à jour diagramme de Gantt du projet –milieu de projet si nécessaire
- Remise d'un plan détaillé du rapport

Semaine 8
21 et 22/2
Soutenances projet tuteuré

I - gestion de projet et travail en équipe



3 bonnes raisons de travailler en groupe

Gagner du
temps

Diviser le travail pour
mutualiser les forces

Gagner en
complexité

Diviser le travail en
articulant les
compétences

Gagner en
pertinence

Cocréer en déployant
l'intelligence collective

Définir et distribuer des rôles



Prendre des décisions



Construire un projet commun



Créer une dynamique de groupe



Travailler en mode collaboratif



Les 9 enjeux du travail en équipe

Partager les informations



Réguler les conflits



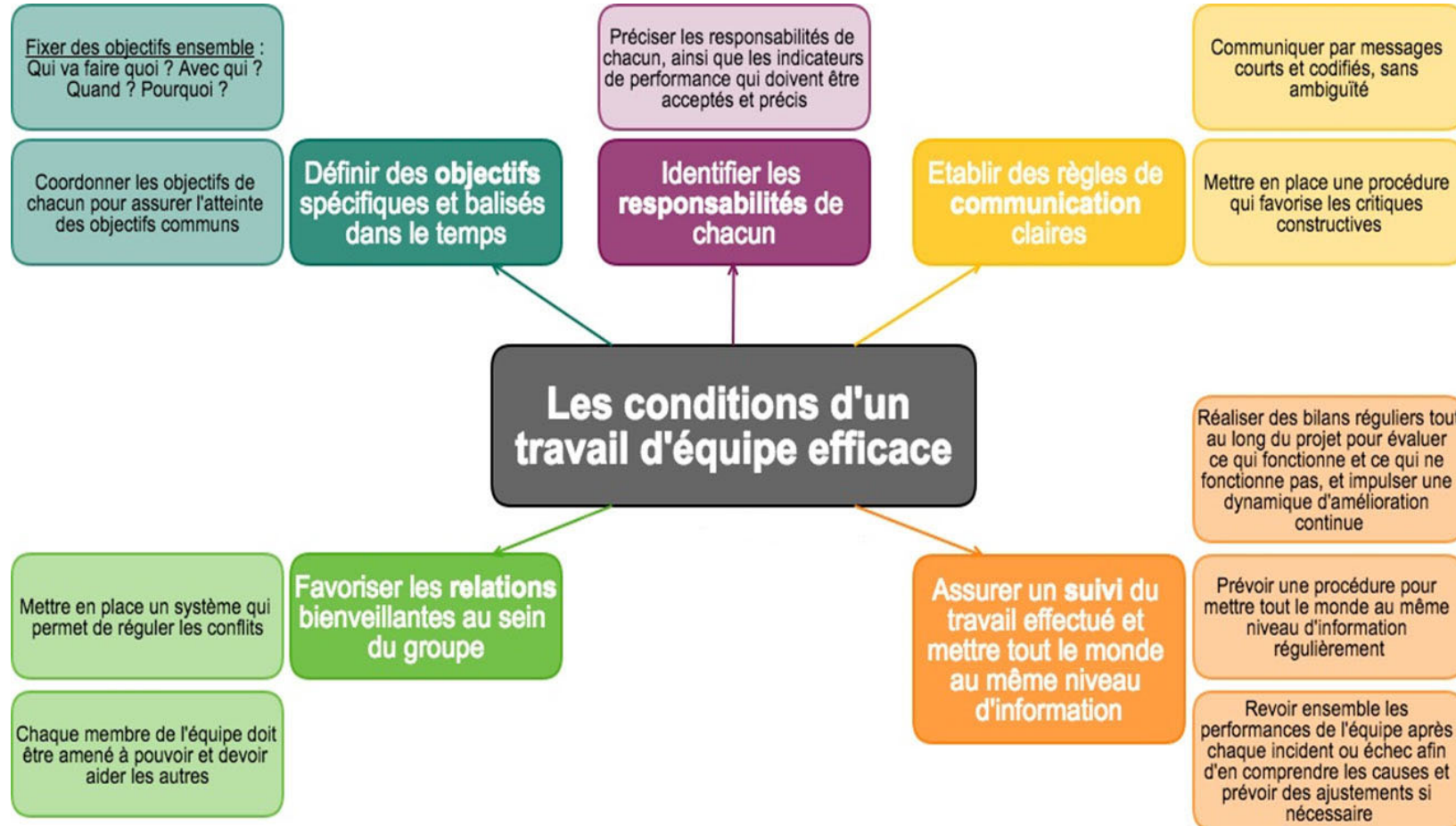
Accueillir de nouveaux membres



Evaluer et célébrer le travail accompli

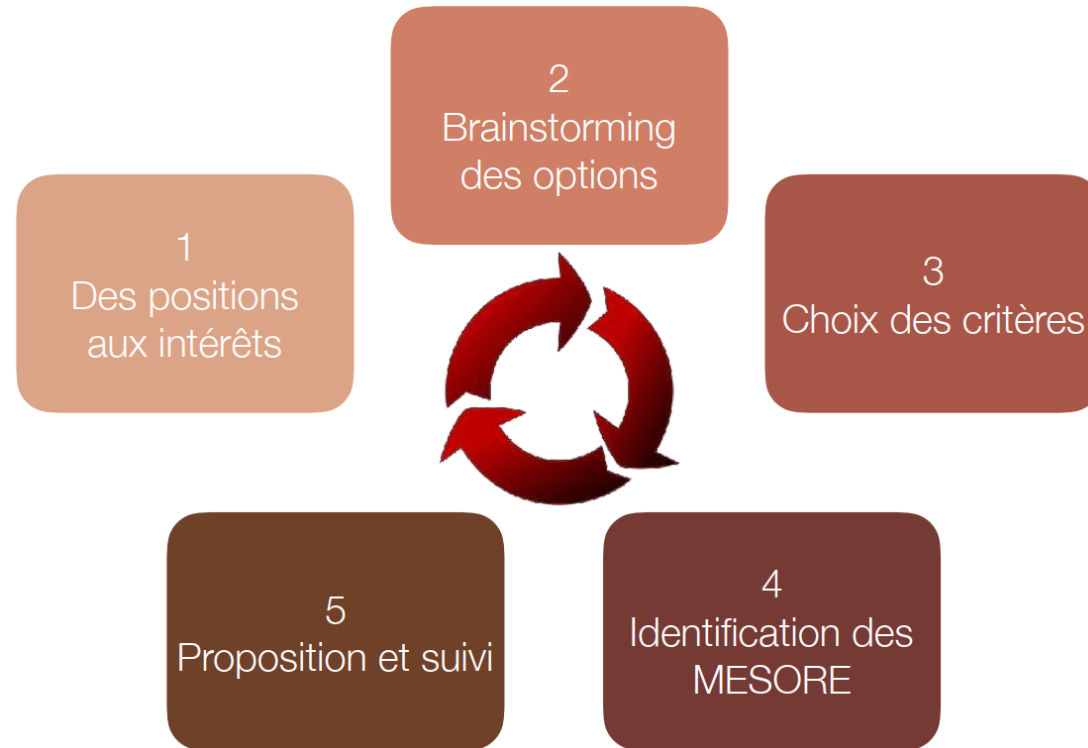


Travailler en équipe



Travailler en équipe

Négocier en cas de conflits



Visionner le module numérique “Apprendre à communiquer en équipe”

https://madoc.univ-nantes.fr/pluginfile.php/1787110/mod_resource/content/11/index.html

+ Test à faire en ligne (semaine 39 au plus tard)

Gabarits de reunion disponibles sur Madoc

Dépôt des compte-rendus des réunions du groupe (au sein du groupe et avec le tuteur) : semaine 45

Puis dans rapport final tous les CR de réunions (du groupe et avec le tuteur): semaine 7 de 2024

1- Gérer ses choses à faire objectivement et les classer (prioriser)

2- Gérer son temps (les planifier)

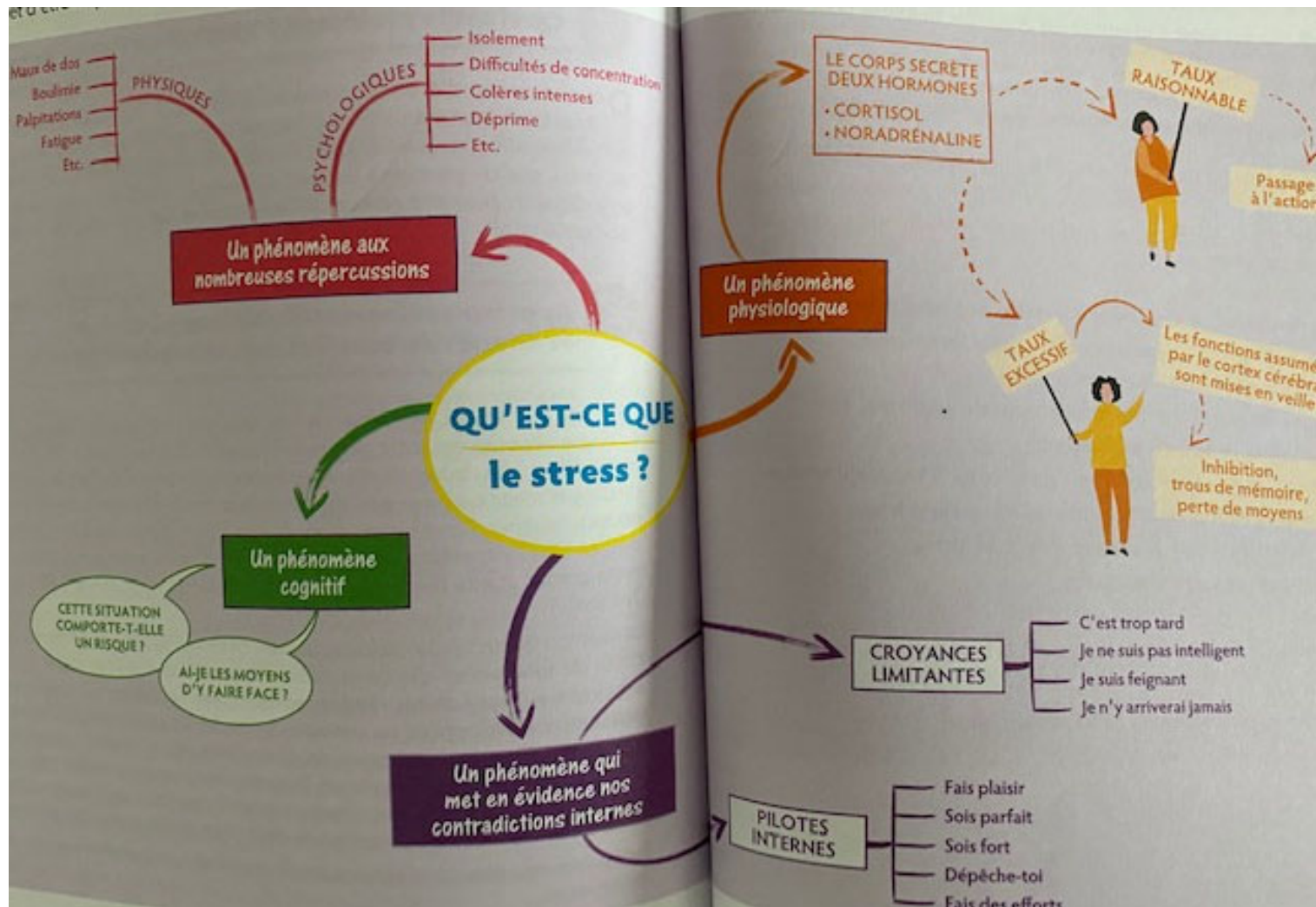
3- Apprivoiser les manifestations physiques et physio du stress (palpitations, blanc, ...) en se remettant en confiance :

- Prise de conscience : lister vos manifestations pour mieux les identifier et agir
- Rituel : nom + prénom + lire tout le sujet; respiration, etc
- Commencer par les points faciles (relance irrigation des autres couches du cerveau : débogage)
- Relativiser : l'idée n'est pas d'avoir 20 mais de faire au mieux

Cours à réaliser en asynchrone par vous-même : Gestion de projet

<https://madoc.univ-nantes.fr/course/view.php?id=32169>

A faire semaines 38- 39



lister objectivement les choses à faire (toutes !) et les planifier ...

fait gagner du temps et est anti-stress !!!

=> *Diagramme de Gant*

Nom de tâche	T1 2009				T2 2009			T3 2009	
	déc. 08	janv. 09	févr. 09	mars 09	avr. 09	mai 09	juin 09	juil. 09	août
Préparation		■	■						
Recherche			■	■					
Conception				■					
Développement					■	■			
Suivi							■		

Visionner les tutos pour Ganttproject
(semaines 37 à 39)

Gantt Project 2.6 :

Tutoriel Université de Lorraine (version 2.6) : <http://dptgeii.iutsd.univ-lorraine.fr/cours/lpsarii/QCP/TUTOGanttProject.pdf>

Tutoriel plus ancien de l'académie Aix-Marseille : https://www.lyc-luynes.ac-aix-marseille.fr/spip/sites/www.lyc-luynes/spip/IMG/pdf/Ganttproject_tutoriel.pdf

vidéos Youtube :

https://www.youtube.com/watch?v=wk_AGveybNs

<https://www.youtube.com/watch?v=U0UdSfsDOj4>

Construction du diagramme de Gantt du projet – version 1 début de projet à déposer sur Madoc
Semaine 40

Mise à jour diagramme de Gantt du projet –milieu de projet à déposer sur Madoc
Semaine 50

II - Recherche bibliographique

Semaine 37

3 Séances à la BU : présentation des outils de recherche biblio Nantilus et de référencement Zotero

Visionner le tuto zotero
semaines 37 à 39

Tutoriel Zotero

Réalisé par l'université de Bordeaux : <https://bibliotheques.u-bordeaux.fr/Se-former/Les-tutoriels/Les-tutos-Zotero>

Cours

Information scientifique:
type, recherche et traitement

I - Pourquoi rechercher de l'information scientifique et techniques (IST)?

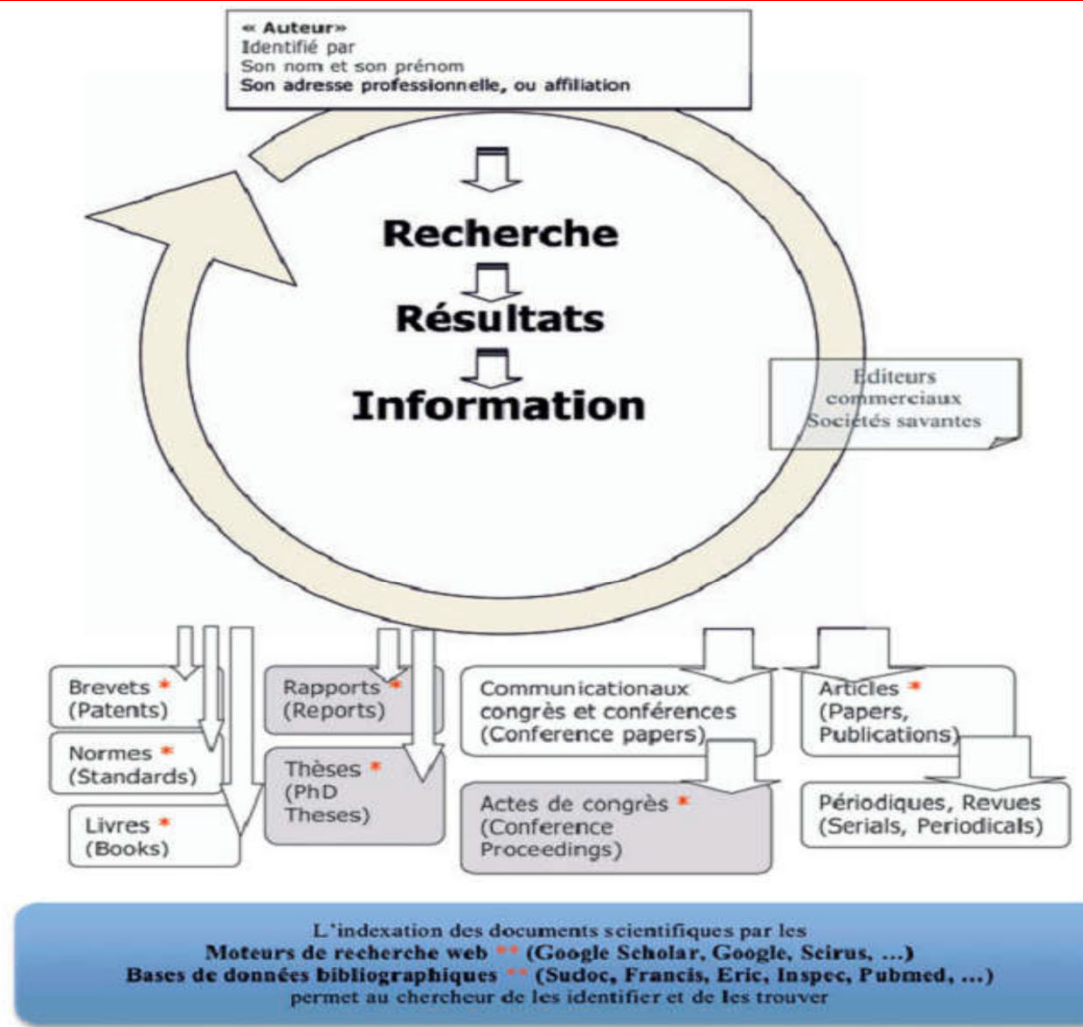
Pourquoi l'industrie a besoin de l'information scientifique ?

- État de l'art sur le sujet traité / protocoles expérimentaux
- Veille technologique / innovation / émergence de nouveaux marchés liés à de nouvelles technologie
- Normalisation

Pourquoi un consultant a besoin de l'information scientifique ?

- Constitution d'un dossier pour un industriel

II – Comment publier de l'information scientifique et techniques (IST)?



Littérature grise : documents diffusés hors des circuits commerciaux.

- * source d'information primaire : contient le texte et les illustrations des auteurs
- ** Source d'information secondaire : donne les références de documents primaires

Types de documents et canaux de publication scientifiques

III – Quel type d’information scientifique et techniques (IST)?

- la « **communication** » ; article non exhaustif sur la recherche menée mais qui présente les principaux résultats
- le « **full article** » ; article détaillé sur la recherche menée (notamment parties expérimentales développées)
- la « **review** » ; article de synthèse sur l’état de l’art dans une thématique donnée, réalisé par une personne dans le domaine
- la **thèse** ; partie bibliographique sur le sujet de la thèse + travaux réalisés par un doctorant pendant sa thèse
- le **livre** ; traitement d’une thématique assez large. Parfois un seul auteur, le plus souvent plusieurs auteurs (par chapitre), chacun traitant de son domaine de compétences
- le **brevet** ; description d’une invention, c’est-à-dire d’un procédé industriel

1 Radiometals for Combined Imaging and Therapy

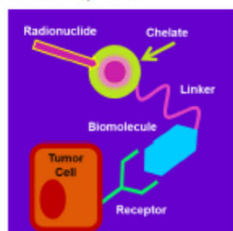
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1. INTRODUCTION

The use of radionuclides in medicine is based largely on the 40
discoveries of two critical concepts, the "tracer principle" and 41
the "magic bullet". In 1913, George de Hevesy developed the 42
tracer approach and was the first to recognize that radionuclides 43
could be used as tracers to follow how the native element or 44
compound containing the element was distributed either in 45
plants or in animals.¹ He based his theory on the principle that 46
radioactivity has the advantage of being easily detected at very 47
low quantities, allowing for the introduction of minute 48
quantities, nano- to picomoles, that will not perturb the 49
system. Thus the radiolabeled tracer allows for noninvasive 50
measurement of distribution and function in a biological 51
system. Paul Ehrlich later developed the "magic bullet" concept 52
highlighting how biomolecules, particularly antibodies, could be 53
utilized as targeting molecules to transport toxins selectively to 54
cancerous tissues. For example, radionuclides can be attached 55
to antibodies that are selective for receptors that are 56
overexpressed on a certain disease site such as tumor cells. 57
This concept has been expanded to include a host of 58
nanocarriers, from small molecules such as folic acid to 59
peptides and proteins, microspheres, and most recently 60
nanoparticles. Both concepts have been utilized to develop 61
radiopharmaceuticals. 62

Radiopharmaceuticals are drugs that consist of two parts: a 63
radionuclide that imparts the mechanism of action through its 64
decay and a targeting biomolecule or organic ligand that 65
determines the localization of the radiopharmaceutical. They 66
can be used either as diagnostics for the noninvasive imaging of 67
disease or as therapeutics to deliver a toxic payload selectively, 68
for instance, to a tumor site. Most of the development and 69
optimization of radiopharmaceuticals occurs when designing or 70
modifying the target selectivity of the molecule, not the 71
mechanism of action, as with other drugs. Diagnostic agents 72
consist of radionuclides that decay to release photons with a 73
high enough energy to penetrate the body and be detected 74
externally but low enough to be collimated by a camera. 75
Therapeutic agents consist of radionuclides that decay to 76
release a particle, such as a β^- or α particle that can cause 77
ionization and break bonds resulting in the intended ablation. 78
Until recently most radiopharmaceuticals were designed to be 79
used solely for either diagnostics or therapeutics. It was thought 80

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accès pdf

Corps de l'article

- Introduction
- Présentation des différents points
- Conclusion
- Références

Plusieurs dizaines de pages

nom du journal (abréviation)

La Communication

accès pdf

ChemComm

RSCPublishing

éditeur

COMMUNICATION

View Article Online
View Journal

type d'article

Efficient asymmetric synthesis of lamivudine via enzymatic dynamic kinetic resolution†

titre

Lei Hu, Fredrik Schaefelberger, Yan Zhang and Claf Ramstrom*

auteurs

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www.rsc.org/chemcomm

date de soumission
+
date d'acceptation

The anti-HIV nucleoside lamivudine was asymmetrically synthesized in only three steps via a novel surfactant-treated subtilisin Carlsberg-catalyzed dynamic kinetic resolution protocol. The enantiomer of lamivudine could also be accessed using the same protocol catalyzed by *Candida antarctica* lipase B.

resolution (DKR) method for the lamivudine synthesis,¹² however requiring not only seven steps of synthesis, and undesirable reagents such as SOCl₂, but also the use of chiral auxiliary-derived starting materials.

DOI : Digital Object Identifier

In the last decade, lamivudine (3TC, 1a) (Fig. 1) has proven to be one of the most successful agents for the treatment of HIV as well as chronic hepatitis B.¹ The compound inhibits both type 1 and type 2 of the human HIV reverse transcriptase and also the reverse transcriptase of hepatitis B *in vitro*.²⁻⁶ As a permanent cure for HIV has remained elusive to date, efficient access to bulk quantities of lamivudine is synthetically very valuable as continuous demand is expected. There are several reported methods to synthesize isomerically pure lamivudine. Most of the previous reports introduced the chiral 1,3-oxathiolane motif by either crystallizing the correct isomer from a racemic mixture,^{7,8} or by enzymatic hydrolysis/acetylation of the other stereoisomers.⁹⁻¹⁴ For example, Liotta and Kossalka developed an efficient six-step pathway to racemic nucleosides and utilized a late-stage enzymatic kinetic resolution with a series of lipases to esterify the undesired enantiomer. Lamivudine was then obtained in good enantiomeric excess but moderate yield.¹⁴ The major disadvantage of these methods is the great loss of yield due to the nature of the kinetic resolution process, as no more than 50% yield could be theoretically achieved while maintaining high enantiomeric purity. In 2005, Goodyear *et al.* employed a crystallization-induced dynamic kinetic

Compared with other commonly used catalysis for asymmetric synthesis, such as chiral coordination complexes and organocatalysis, biocatalysis is now becoming a highly potent alternative in both academia and the pharmaceutical industry.¹⁵⁻²⁶ This is in part due to the high stereoselectivities that can be obtained, the potential to modify/optimize the performances through directed evolution protocols, the inherent environmentally benign (green) nature of the catalysts, and the ease of recycling processes.¹⁷⁻²⁵ In this study, we report a highly efficient three-step asymmetric synthesis of lamivudine and its enantiomer through a novel enzyme-catalyzed DKR protocol based on reversible formation of the intermediate stereoisomers. The key enantioenriched 1,3-oxathiolane structure was obtained in good yield and enantiopurity from two achiral starting materials through an enzyme-catalyzed cascade addition-cyclization-acetylation reaction, leading directly to a suitable substrate for the subsequent Vorbrüggen coupling reaction that is most frequently used for nucleoside synthesis. The advantage of this strategy is obvious, as the formation of the hemiacetal and its transformation into a better leaving group for the subsequent coupling are performed in one pot. In addition, by using different types of enzymes, the stereochemical configuration of the oxathiolane intermediate could be easily controlled, dynamically yielding the precursor of lamivudine or its enantiomer (Fig. 1) respectively. This sets up a useful example for the construction of highly enantioenriched oxathiolane-based nucleosides with access to both enantiomers in a short synthetic route. The method represents an improvement to the previous lamivudine syntheses with respect to both efficiency and environmental friendliness.

résumé
(abstract)

corps de l'article :
- introduction
- résultats et discussion
- conclusion
- notes et références
- supp. material (web)

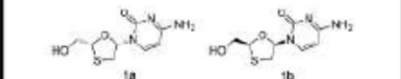


Fig. 1 Lamivudine (1a) and its enantiomer (1b).

Taking advantage of the dynamic formation of hemithioacetals,^{26,27} we recently reported that *Candida antarctica* lipase B (CAL B) catalyzes the cyclization of the intermediate generated from the reversible nucleophilic addition of sulfolactate 2 to methylene 3, asymmetrically forming 1,3-oxathiolan-5-one derivative 4 (Scheme 1).²⁸ Since the core structures of compounds 1 and 4 are

coordonnées des auteurs

de 1 à 5 pages

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A Novel Bispecific, Trivalent Antibody Construct for Targeting Pancreatic Carcinoma

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Abstract

Preliminary and clinical studies have demonstrated the application of radiolabeled mAb-PAM4 for nuclear imaging and radioimmunotherapy of pancreatic carcinoma. We have now examined the ability of a novel PAM4-based, bispecific monoclonal antibody (mAb) construct, TF10, to pretarget a radiolabeled peptide for improved imaging and therapy. TF10 is a humanized, bispecific mAb, divalent for mAb-PAM4 and monovalent for mAb-679, reactive against the histamine-succinyl-glycine hapten. Biodistribution studies and nuclear imaging of the radiolabeled TF10 and/or TF10-pretargeted hapten-peptide (IMP-288) were conducted in nude mice bearing CaPan1 human pancreatic cancer xenografts. ¹²⁵I-TF10 cleared rapidly from the blood, with levels decreasing to <1% injected dose per gram (ID/g) by 16 hours. Tumor uptake was 3.47 ± 0.66% ID/g at this time point with no accumulation in any normal tissue. To show the utility of the pretargeting approach, ¹¹¹In-IMP-288 was administered 16 hours after TF10. At 3 hours postadministration of radiolabeled peptide, imaging showed intense uptake within the tumors and no evidence of accretion in any normal tissue. No targeting was observed in animals given only the ¹¹¹In-peptide. Tumor uptake of the TF10-pretargeted ¹¹¹In-IMP-288 was 24.3 ± 1.7% ID/g, whereas for ¹¹¹In-IMP-288 alone it was only 0.12 ± 0.002% ID/g at 16 hours. Tumor/blood ratios were significantly greater for the pretargeting group (~1,000:1 at 3 hours) compared with ¹¹¹In-PAM4-IgG (~5:1 at 24 hours; *P* < 0.0003). Radiation dose estimates suggested that TF10-⁹⁰Y-peptide pretargeting would provide a greater antitumor effect than ⁹⁰Y-PAM4-IgG. Thus, the results suggest that TF10 pretargeting may provide improved imaging for early detection, diagnosis, and treatment of pancreatic cancer as compared with directly radiolabeled PAM4-IgG. [Cancer Res 2008;68(12):4819-26]

Introduction

Pancreatic cancer is an insidious disease with a particularly high mortality rate. In large measure, this is due to the location of the pancreas in the retroperitoneum, where the tumor can grow in a silent fashion. Symptoms that might suggest the patient seek medical assistance are usually not evident until an advanced stage

of tumor growth, and even at this time, the clinical presentation can be vague and representative of varying pathologies. Combined with the fact that at present, there are no effective means for treatment of this disease, patient outcomes are generally poor; 5-year survival is <5%. However, if detected early when the cancer is still restricted to the pancreas, treatment by surgical resection, with or without chemotherapy and radiation therapy, can improve 5-year survival to roughly 25%; yet even this statistic is not very encouraging (1, 2). Consequently, considerable effort has been undertaken to find new methods to detect pancreatic cancer at an early stage of tumor growth (pancreatic intraepithelial neoplasia (3)) before it becomes invasive, and to improve survival through earlier and more effective treatments.

We have identified a unique biomarker present on mucin expressed by >85% of invasive pancreatic adenocarcinomas, including early stage I disease and the precursor lesions, pancreatic intraepithelial neoplasia and intraductal papillary mucinous neoplasia (3). The specific epitope, as detected by mAb-PAM4 (4), is absent from normal and inflamed pancreatic tissues, as well as most other malignant tissues. Thus, detection of the epitope provides a high diagnostic likelihood for the presence of pancreatic neoplasia. Early clinical studies using ¹³¹I- and ^{99m}Tc-labeled, murine PAM4 IgG or Fab', respectively, showed specific targeting in 8 of 10 patients with invasive pancreatic adenocarcinoma (5, 6). Of the two negative studies, one had a poorly differentiated pancreatic carcinoma that did not express the PAM4-epitope, whereas the other patient was later found to have pancreatitis rather than a malignant lesion. Accordingly, we believe that the high specificity of PAM4 for pancreatic cancer could be helpful in the detection and diagnosis of early disease. In addition to improved detection, ⁹⁰Y-PAM4 IgG was found to be effective in treating large human pancreatic cancer xenografts in nude mice (7), and when combined with gemcitabine, further improvements in therapeutic response were observed (8, 9). A Phase I therapy trial in patients who failed gemcitabine treatment was recently completed, finding the maximum tolerated dose of ⁹⁰Y-humanized PAM4 IgG to be 20 mCi/m² (10). Although all patients showed disease progression at or after week 8, initial shrinkage of tumor was observed in several cases. Clinical studies are now underway to evaluate a fractionated dosing regimen of ⁹⁰Y-hPAM4 IgG in combination with a radiosensitizing dose of gemcitabine.

Preliminary studies in xenograft models of colorectal cancer and lymphoma have suggested that delivery of radionuclides with pretargeting procedures can provide a significant therapeutic advantage over directly radiolabeled antibodies (11-16). In addition, we have shown that pretargeting procedures can be used in combination with ^{99m}Tc or ¹²⁵I for superior imaging capability over directly radiolabeled antibody fragments (17, 18). Thus, a pretargeting system based on the specificity of PAM4 for pancreatic

Note: Supplementary data for this article are available at Cancer Research Online (<http://cancerres.aacrjournals.org>).

Requests for reprints: David V. Gold, Garden State Cancer Center, 210 Belleville Avenue, Belleville, NJ 07109. Phone: 973-844-7025; Fax: 1-973-844-7026; E-mail: dgold@gscancer.org.

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Full article

accès pdf

Corps de l'article

- Introduction
- Description expérimentale
- Présentation des résultats
- Discussion
- Conclusion
- Références
- Suppl. material

de 5 à 10 pages

TRAP, a Powerful and Versatile Framework for Gallium-68 Radiopharmaceuticals**

Johannes Notni,^[a] Jakub Šimeček,^[a, b] Petr Hermann,^[b] and Hans-Jürgen Wester^[a]

Dedicated to Prof. em. Dr. rer. nat. habil. Ernst Anders on the occasion of his 70th birthday

The remarkable success of ^{68}Ga -labeled peptides in neuroendocrine tumor diagnostics gave a major boost to the development of ^{68}Ga -labeled tracers for positron emission tomography (PET).^[1a] In contrast to common PET isotopes, ^{68}Ga ($t_{1/2} = 68 \text{ min}$; $E_{\beta^+} = 1.89 \text{ MeV}$) is not produced by on-site cyclotrons but, similarly to $^{99\text{m}}\text{Tc}$ production for scintigraphy, is obtained from $^{68}\text{Ge}/^{68}\text{Ga}$ radioisotope generators ($t_{1/2} (^{68}\text{Ge}) = 270.8 \text{ days}$). Conjugation of biologically active molecules to bifunctional chelate ligands and subsequent $^{68}\text{Ga}^{3+}$ complexation delivers radiopharmaceuticals that bind to pathologically overexpressed target structures with high affinity and thus allow for non-invasive molecular imaging in patients.

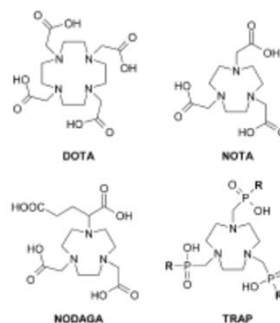
Until now, the design of ^{68}Ga tracers mainly relied on DOTA^[1] (Scheme 1), which is ideally suited for larger metal ions (particularly lanthanides) but less so for the smaller Ga^{3+} ion. However, the utility of the smaller NOTA^[2] system (Scheme 1) for Ga^{3+} complexation has been shown two decades ago.^[2] As it has been found that it forms Ga^{3+} complexes with higher kinetic stability and allows higher ^{68}Ga labeling yield, conjugates of some of its bifunctional derivatives (mainly NODAGA^[2b] Scheme 1) are increasingly utilized in the development of ^{68}Ga radiopharmaceuticals in recent times. Inspired by these results, we report here the synthesis, properties, and preclinical evaluation of ^{68}Ga radiopharmaceuticals derived from NOTA-analogous Tri-Azacyclononane-Phosphinic acids^[3] (abbreviated TRAP; see Scheme 1 and Table 1) and reveals their enormous utility for nuclear medicine and molecular imaging.

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** TRAP = Triazacyclononane-phosphinic acid.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/chem.201103503>.



Scheme 1. Macrocyclic chelators discussed in the text (see also Table 1).

Table 1. TRAP ligands used in this study.

Identifier	Substituent R (Scheme 1)	Ref.
TRAP-H	H	[4]
TRAP-Ph	Ph	[5a]
TRAP-OH	$\text{CH}_2\text{-OH}$	[1]
TRAP-Pr	$\text{CH}_2\text{-CH}_2\text{-COOH}$	[1]

The $^{68}\text{Ga}^{3+}$ complexation behavior was compared for TRAP ligands (Table 1), DOTA, and NOTA. Figure 1 shows that TRAP ligands are able to incorporate ^{68}Ga nearly quantitatively (> 95 %) at much lower ligand concentrations (c_L) and, due to the low $\text{p}K_a$ of phosphinic acid moieties (ca. 0.7–1.5^[4,5]), also in strongly acidic media; in the case of TRAP-OH^[4] and TRAP-Pr^[5] even at a pH as low as 0.5. As this allows ^{68}Ga labeling by directly using the neat eluate (0.1 M HCl) of the very popular Obninsk generator, greatly facilitated kit production of ^{68}Ga tracers could be achieved. Figure 2 illustrates that particularly TRAP-Pr rapidly incorporates ^{68}Ga at 25 °C and $c_L = 3 \mu\text{M}$, whereas neither DOTA nor NOTA can be labeled under these conditions. However, in line with previous reports^[2d] we found that unlike DOTA, NOTA can be readily labeled at room temperature when using a fairly high ligand concentration of $c_L = 100 \mu\text{M}$ (see the Supporting Information for details).

Supporting Information

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TRAP, a Powerful and Versatile Framework for Gallium-68 Radiopharmaceuticals**

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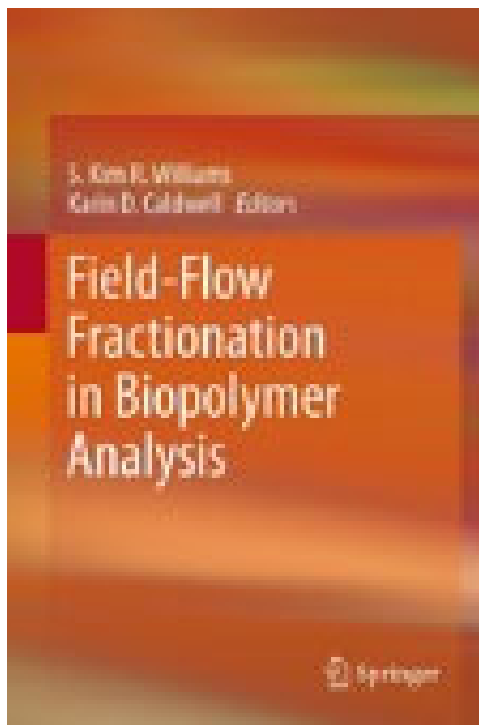


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Spécialité : Chimie

Etude structurale des polysaccharides pariétaux de l'algue rouge *Asparagopsis armata* (Bonnemaisoniales)

Présentée par

Sandrine GARON-LARDIERE

Soutenue le 24 février 2004

Devant le jury composé de

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Corps de l'article


- Introduction
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100 à 200 pages

F – Le brevet (patent)

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(54) **NOUVEAU PROCÉDE DE PREPARATION D'INTERMÉDIAIRES DE SYNTHÈSE**
VERFAHREN ZUR HERSTELLUNG VON ZWISCHENPRODUKTEN FÜR SYNTHÈSE
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(86) Documents cités:
EP-A- 8 178 553
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- **KAPTEIN, BERNARD ET AL:** "Enzymic resolution of alpha...alpha...disubstituted alpha...amino acid esters and amides" **TETRAHEDRON: ASYMMETRY** (1993), 4(6), 1113-16 CODEN: TASYE3;ISSN: 0957-4166, 1993, XP002091821 cité dans la demande
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US006331547B1

(12) **United States Patent**
Zhu et al.(10) **Patent No.:** US 6,331,547 B1
(45) **Date of Patent:** Dec. 18, 2001(54) **WATER SOLUBLE SDZ RAD ESTERS**(75) **Inventors:** Tianmin Zhu, Monroe, NY (US); Syed M. Shah, East Hanover, NJ (US); Richard W. Saunders, Palisades, NY (US)(73) **Assignee:** American Home Products Corporation, Madison, NJ (US)(*) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.(21) **Appl. No.:** 09/639,610(22) **Filed:** Aug. 16, 2000**Related U.S. Application Data**

(60) Provisional application No. 60/183,035, filed on Aug. 18, 1999.

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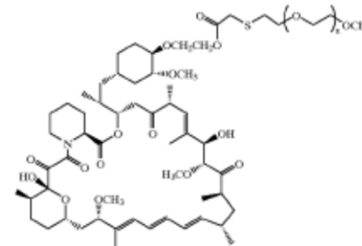
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Primary Examiner—Bruck Kille(74) *Attorney, Agent, or Firm*—Arnold S. Milowsky(57) **ABSTRACT**

This invention provides novel water soluble pegylated esters of rapamycin, having the general structure:



wherein n is an integer from about 5 to about 450, as well as pharmaceutical compositions containing these compounds and methods for their use as immunosuppressive, anti-inflammatory, antifungal, antiproliferative and antitumor agents.

18 Claims, No Drawings

Intérêt des différentes formes de littérature

⇒ le livre, la revue :

- + permet de se faire une idée globale sur la thématique
- pas de détail expérimental
- selon l'année de la publication, pas forcément à jour

⇒ le full paper :

- + permet d'avoir une description expérimentale précise
- pas forcément représentatif des techniques en cours si trop ancien

⇒ la communication :

- + si récente, permet de voir les dernières tendances
- si trop ancienne, moins d'intérêt

⇒ le brevet :

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- toute application industrielle n'est pas forcément brevetée (secret industriel)

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- ⇒ Avant de commencer la recherche :
 - quelle est la question posée
 - quel aspect du sujet souhaitons-nous aborder
 - quels aspects exclure
 - quels sont les mots clés les plus pertinents
 - quel type de document (livre, thèse, revue, article, brevet...)

- ⇒ Recueillir la documentation choisie : pertinence, lecture critique...

- ⇒ Trier l'information sur des critères objectifs et sur des données validées

- ⇒ Synthétiser et organiser

- ⇒ Coût en temps et en argent (selon les cas)

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- 2) Trouver des livres et des revues pour cerner le sujet**
- 3) Voir les dernières évolutions avec des articles récents**

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Measurement of ^{43}Sc and ^{44}Sc production cross-section with an 18 MeV medical PET cyclotron

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HIGHLIGHTS

- The production cross sections of Sc-43 and Sc-44 by proton irradiation were measured.
- The thick target production yields and purities were evaluated.
- Method based on irradiating the whole target by constant surface density proton beam.
- Measurements performed using a beam transfer line and a 18 MeV medical PET cyclotron.

ARTICLE INFO

Keywords:
 PET radiotopes
 Medical cyclotrons
 Scandium
 Cross-section
 Positron Emission Tomography (PET)

ABSTRACT

^{43}Sc and ^{44}Sc are positron emitter radionuclides that, in conjunction with the β^- emitter ^{47}Sc , represent one of the most promising possibilities for theranostics in nuclear medicine. Their availability in suitable quantity and quality for medical applications is an open issue and their production with medical cyclotrons represents a scientific and technological challenge. For this purpose, an accurate knowledge of the production cross sections is mandatory. In this paper, we report on the cross section measurement of the reactions $^{43}\text{Ca}(p,n)^{43}\text{Sc}$, $^{44}\text{Ca}(p,2n)^{43}\text{Sc}$, $^{44}\text{Ca}(p,n)^{44}\text{Sc}$ and $^{44}\text{Ca}(p,n)^{44}\text{Sc}$ at the Bern University Hospital cyclotron. A study of the production yield and purity performed by using commercially available enriched target materials is also presented.

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THESE de DOCTORAT de l'UNIVERSITE PARIS XI

Spécialité :
CHIMIE

présentée par

Lucie BONIN

pour obtenir le grade de DOCTEUR de l'UNIVERSITE PARIS XI

**Etude de la spéciation des actinides vis-à-vis de ligands d'intérêt
pour la décorporation**

Soutenue le 11 janvier 2008 devant la commission d'examen

M. B. Grambow
M. S. Nikitenko

Rapporteur
Rapporteur

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M. M. Leroy
M. Ph. Moisy
M. E. Simoni

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M. A. Ananyev

Membre invité

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