SUPPLEMENTARY INFORMATION

Targeting the 3CLpro and RdRp of SARS-CoV-2 with phytochemicals from medicinal plants of the Andean region: molecular docking and molecular dynamics simulations

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Supplementary Table 1

Docking scores of tested ligands

Ligand	PUBCHEM ID or DrugBank ID	Docking score (kcal/mol) to SARS-CoV-2 target		Source in the Andean region	Reference
		3CLpro	RdRp		
1,3,5-Trimethoxybenzene	69301	-4.5	-4.4	*Croton lechleri*	(Lock, Perez, Villar, Flores, & Rojas, 2016)
18,19-Dihydrocorynantheine	3039336	-6.1	-6.0	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
246-Trimethoxyphenol	88563	-6.0	-4.6	*Croton lechleri*	(Lock et al., 2016)
4-Hydroxycinnamic acid	637542	-5.1	-5.2	*Clinopodium tomentosum*	(Vera Saltos, Naranjo-Puente, Malafronte, & Braca, 2014)
8-prenyldaidzein	14841119	-7.3	-7.0	*Erythrina fusca*	(Khaomek et al., 2008)
Alpha-Pinene	6654	-4.3	-4.6	*Minthostachys mollis*	(Torrenegra-Alarcon et al., 2016)
Apigenin	5280443	-7.7	-6.6	*Physalis peruviana*	(El-Beltagi, Mohamed, Safwat, Gamal, & Megahed, 2018)
Betulinic acid	64971	-7.4	-7.2	*Conyza floribunda*	(Manguro, Ogur, & Opiyo, 2010)
Bicyclogermacrene	13894537	-5.2	-5.4	*Minthostachys mollis*	(Torrenegra-Alarcon et al., 2016)
Byzantionoside B	14135395	-7.6	-6.9	*Clinopodium tomentosum*	(Vera Saltos et al., 2014)
Caffeic acid	689043	-5.6	-5.7	*Clinopodium tomentosum*	(Vera Saltos et al., 2014)
Carvacrol	10364	-4.3	-4.8	*Minthostachys mollis*	(Torrenegra-Alarcon et al., 2016)

Cinchonidine	101744	-7.5	-6.5	*Cinchona officinalis*	(Murauer & Ganzera, 2018)
Cinchonine	90454	-6.8	-6.4	*Cinchona officinalis*	(Murauer & Ganzera, 2018)
Corosolic acid	6918774	-8.7	-8.3	*Ugni molinae*	(Goity-Vivar, 2013)
Corynoxeine	44568160	-6.4	-6.5	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Cristacarpin	126540	-7.7	-7.0	*Erythrina fusca*	(Innok, Rukachaisirikul, & Suksamrarn, 2009)
Crolechinic acid	102237419	-6.4	-6.4	*Croton lechleri*	(Lock et al., 2016)
Cyasterone	119444	-7.9	-8.0	*Conyza floribunda*	(Manguro et al., 2010)
Cycloeucalenol	101690	-6.2	-7.2	*Croton elegans*	(Herrera et al., 2018)
D-limonene	440917	-4.5	-4.5	*Minthostachys mollis*	(Torrenegra-Alarcon et al., 2016)
Dolichin A	44257432	-7.5	-7.3	*Erythrina fusca*	(Innok et al., 2009)
Dolichin B	44257433	-7.6	-6.5	*Erythrina fusca*	(Innok et al., 2009)
Enhydrin	5281441	-6.1	-6.0	*Smallanthus sonchifolius*	(Lin, Hasegawa, & Kodama, 2003)
Erythrisenegalone	15224381	-7.8	-7.5	*Erythrina fusca*	(Khaomek et al., 2008)
Fluctuanin	101250074	-5.8	-5.8	*Smallanthus sonchifolius*	(Lin et al., 2003)
Friedelin	91472	-8.3	-8.2	*Croton elegans*	(Herrera et al., 2018)
Gallic acid	370	-5.5	-5.9	*Physalis peruviana*	(El-Beltagi et al., 2018)
Germacrene-D	91723653	-5.1	-5.1	*Minthostachys mollis*	(Torrenegra-Alarcon et al., 2016)
Glaucine	16754	-7.1	-6.3	*Croton lechleri*	(Lock et al., 2016)
Glucotropaeolin	656498	-7.0	-6.5	*Lepidium meyenii*	(Sifuentes-Penagos, León-Vásquez, & Paucar-Menacho, 2015)
Guaijaverin	5481224	-8.6	-7.2	*Bauhinia longifolia*	(dos Santos et al., 2014)
Harmaline	3564	-6.3	-6.0	*Banisteriopsis caapi*	(Callaway, 2005)
Hesperetin	72281	-7.3	-7.0	*Clinopodium tomentosum*	(Vera Saltos et al., 2014)
Hesperidin	10621	-8.8	-8.6	*Psidium guajava*	(Trujillo-Correa et al., 2019)
Hirsutine	3037884	-6.5	-6.5	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Hirsuteine	3037151	-6.1	-6.0	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Hyperin	5281643	-8.6	-7.1	*Bauhinia longifolia*	(dos Santos et al., 2014)

Isobavachalcone	5281255	-8.1	-6.6	*Erythrina fusca*	(Innok et al., 2009)
Isoboldine	133323	-7.6	-6.7	*Croton lechleri*	(Lock et al., 2016)
Isocorynoxeine	3037448	-7.0	-6.9	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Isomitraphylline	11726520	-7.2	-7.0	*Conyza floribunda*	(Manguro et al., 2010)
Isoquercitrin	5280804	-8.1	-7.2	*Bauhinia longifolia*	(dos Santos et al., 2014)
Isorhynchophylline	3037048	-6.2	-6.9	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Isorotundifoline	102232176	-6.4	-6.2	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Kaempferol	5280863	-7.7	-7.1	*Conyza floribunda*	(Manguro et al., 2010)
Korberin A	101926685	-6.4	-6.9	*Croton lechleri*	(Lock et al., 2016)
Limonene	22311	-4.4	-4.6	*Minthostachys mollis*	(Torrenegra-Alarcon et al., 2016)
Lonchocarpol A	124035	-8.0	-7.4	*Erythrina fusca*	(Innok et al., 2009)
Longifolol	78265163	-5.3	-5.5	*Minthostachys mollis*	(Torrenegra-Alarcon et al., 2016)
Lupinifolin	10250777	-8.3	-7.6	*Erythrina fusca*	(Innok et al., 2009)
Macaridine	636583	-5.7	-5.6	*Lepidium meyenii*	(Sifuentes-Penagos et al., 2015)
Magnoflorine	73337	-7.6	-6.6	*Croton lechleri*	(Lock et al., 2016)
Mangiferin	5281647	-8.4	-8.4	*Arrabidaea samydoides*	(Brandao et al., 2009)
Methylpallidine	10405046	-6.8	-6.4	*Bauhinia longifolia*	(dos Santos et al., 2014)
Minquartynoic acid	183614	-5.4	-5.3	*Minquartia guianensis*	(de Carvalho-Cursino, Nunez, de Paula, Alves-do Nascimento, & dos Santos, 2012)
Mitraphylline	94160	-7.7	-6.9	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Myricetin	5281672	-7.3	-7.1	*Conyza floribunda*	(Manguro et al., 2010)
N,N-Dimethyltryptamine	6089	-5.2	-4.9	*Psychotria viridis*	(Blackledge & Taylor, 2003)
Naringenin	932	-7.6	-6.6	*Physalis peruviana*	(El-Beltagi et al., 2018)
Neurolobatin A	76317958	-7.3	-6.5	*Neurolaena lobata*	(Lajter et al., 2014)
Neurolobatin B	76332514	-7.4	-6.4	*Neurolaena lobata*	(Lajter et al., 2014)
Norisoboldine	14539911	-7.8	-6.9	*Croton lechleri*	(Lock et al., 2016)
Notholaenic acid	3085829	-7.2	-6.3	*Notholaena nivea*	(Cioffi et al., 2011)

Oleanolic acid	10494	-7.7	-8.3	*Minquartia guianensis* *Uncaria tomentosa*	(Gonzales & Valerio, 2006; de Carvalho-Cursino et al., 2012)
Pallidine	12313923	-7.0	-6.9	*Bauhinia longifolia*	(dos Santos et al., 2014)
Phaseollidin	119268	-7.4	-7.2	*Erythrina fusca*	(Innok et al., 2009)
Pinocembrin 7-O-rutinoside	189596	-8.5	-8.8	*Clinopodium tomentosum*	(Vera Saltos et al., 2014)
Pulegone	442495	-5.0	-4.9	*Minthostachys mollis*	(Torrenegra-Alarcon et al., 2016)
Quercetin	5280343	-7.3	-7.3	*Bauhinia longifolia*	(dos Santos et al., 2014)
Quercitrin	5280459	-9.0	-8.0	*Bauhinia longifolia*	(dos Santos et al., 2014)
Quinidine	441074	-6.8	-6.4	*Cinchona officinalis*	(Murauer & Ganzera, 2018)
Quinine	3034034	-7.0	-6.6	*Cinchona officinalis*	(Murauer & Ganzera, 2018)
Rhynchophylline	5281408	-6.4	-6.3	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Rosmaniric acid	5281792	-7.8	-6.3	*Clinopodium tomentosum*	(Vera Saltos et al., 2014)
Rotundifoline	139055911	-6.6	-6.2	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Rutin	5280805	-8.9	-8.5	*Croton lechleri* *Physalis peruviana*	(Lock et al., 2016) (Toro, Aragon, Ospina, Ramos, & Castellanos, 2014)
Sandwicensin	467498	-7.1	-6.6	*Erythrina fusca*	(Innok et al., 2009)
Sinoacutin	821366	-7.3	-6.6	*Croton lechleri*	(Lock et al., 2016)
Speciophylline	168985	-7.2	-7.7	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Squalene	638072	-5.9	-4.6	*Minquartia guianensis*	(de Carvalho-Cursino et al., 2012)
Stigmasterol	5280794	-7.1	-7.3	*Lepidiun meyenii* *Uncaria tomentosa*	(Gonzales & Valerio, 2006; Sifuentes-Penagos et al., 2015)
Taspine	215159	-7.7	-6.9	*Croton lechleri*	(Lock et al., 2016)
Tetrahydroalstonine	72340	-7.5	-7.2	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Thaliporphine	100020	-7.3	-6.4	*Croton lechleri*	(Lock et al., 2016)
Tomentoside	101664499	-7.5	-6.9	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Uncarine B	12304286	-7.6	-7.2	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)

Uncarine C	10429112	-7.9	-6.9	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Uncarine F	12304288	-7.6	-6.5	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Uvedalin	73353398	-6.4	-6.5	*Uncaria tomentosa*	(Gonzales & Valerio, 2006)
Vitexin	5280441	-8.1	-8.9	*Croton lechleri*	(Lock et al., 2016)
Wighteone	5281814	-7.3	-7.0	*Erythrina fusca*	(Pino-Rodriguez et al., 2004)
Chloroquine	2719	-6.0	-5.0		
Hydroxychloroquine	3652	-6.3	-5.6		
Darunavir	DB01264	-7.7	-7.9		
Lopinavir	DB01601	-7.9	-6.9		
Nelfinavir	DB00220	-8.3	-7.9		
Paritaprevir	DB09297	-10.3	-12.3		
Remdesivir	DB14761	-8.2	-7.5		
Ritonavir	DB00503	-8.2	-7.2		
Saquinavir	DB01232	-7.8	-7.6		
Setrobuvir	DB12051	-9.4	-8.7		
Simeprevir	DB06290	-9.3	-9.3		
Sofosbuvir	DB08934	-8.1	-7.4		

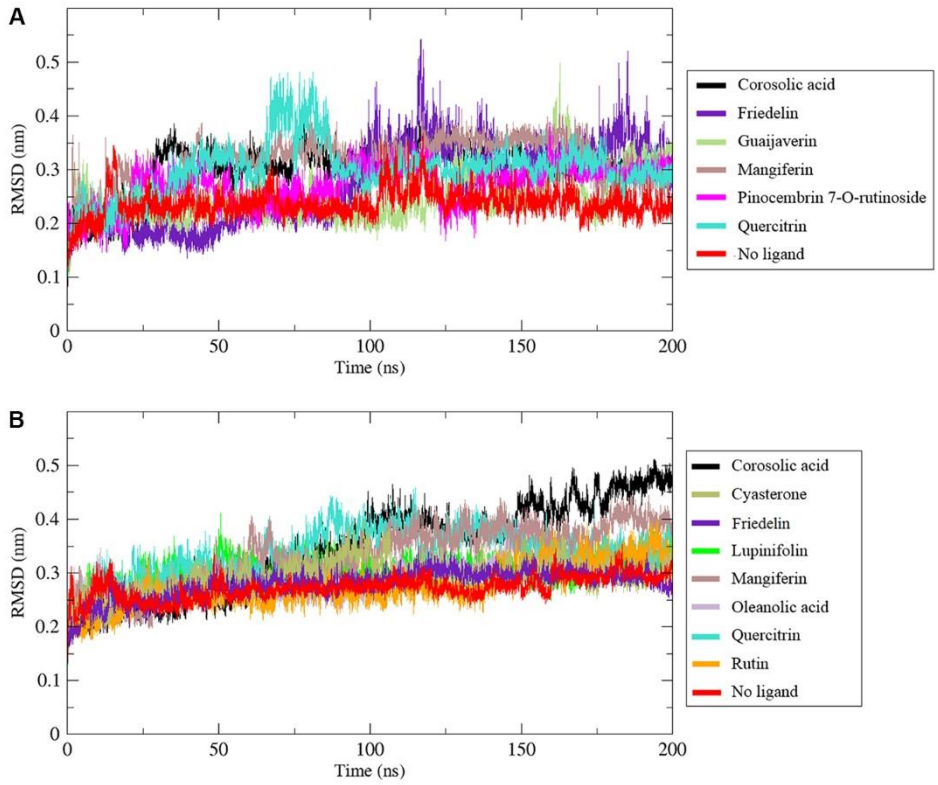

Figure S1. Backbone root mean square deviation (RMSD) of the 3CLpro (A) and RdRp (B) of SARS-CoV-2 in complex with phytochemicals, during 200 ns of the molecular dynamics simulation period. Backbones with mean RMSD higher than free protein are plotted.

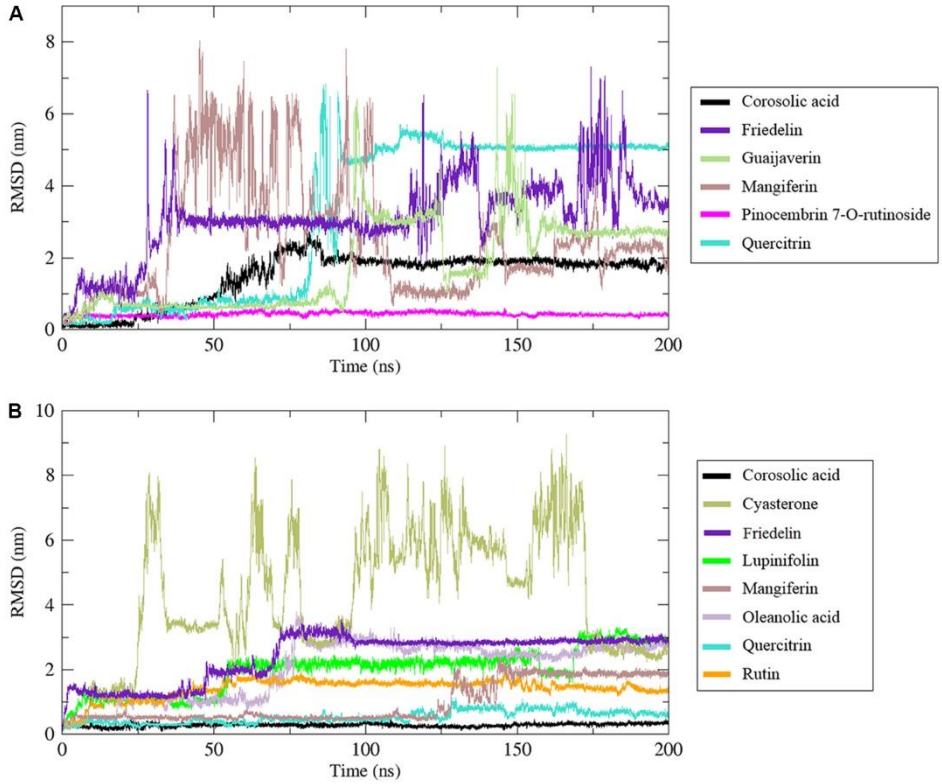

Figure S2. Backbone root mean square deviation (RMSD) of phytochemicals from complexes with 3CLpro (A) and RdRp (B), during 200 ns of the molecular dynamics simulation period.

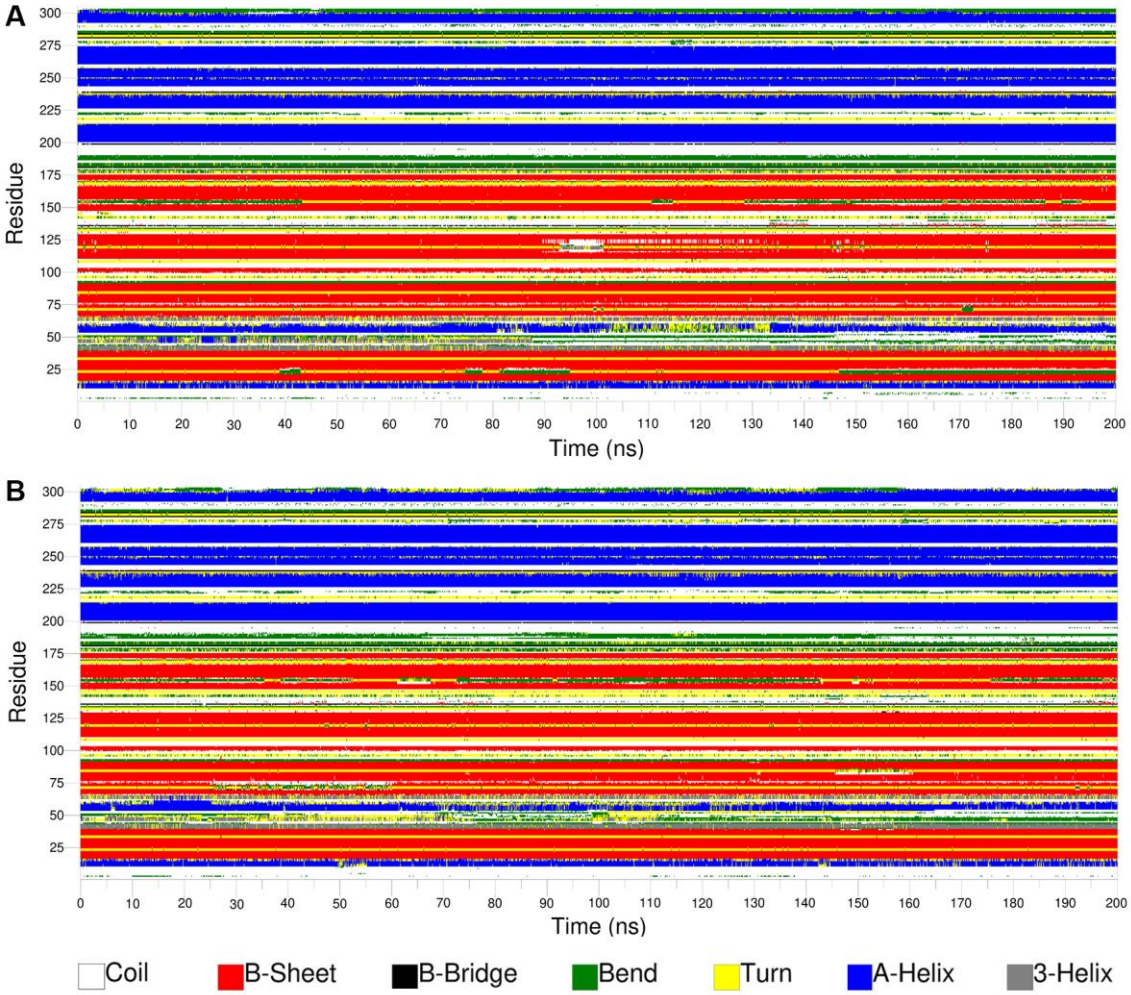

Figure S3. Conformational evolution of secondary structure elements of 3CLpro in complex with hesperidin (A) and lupinifolin (B) during the molecular dynamics simulation period.

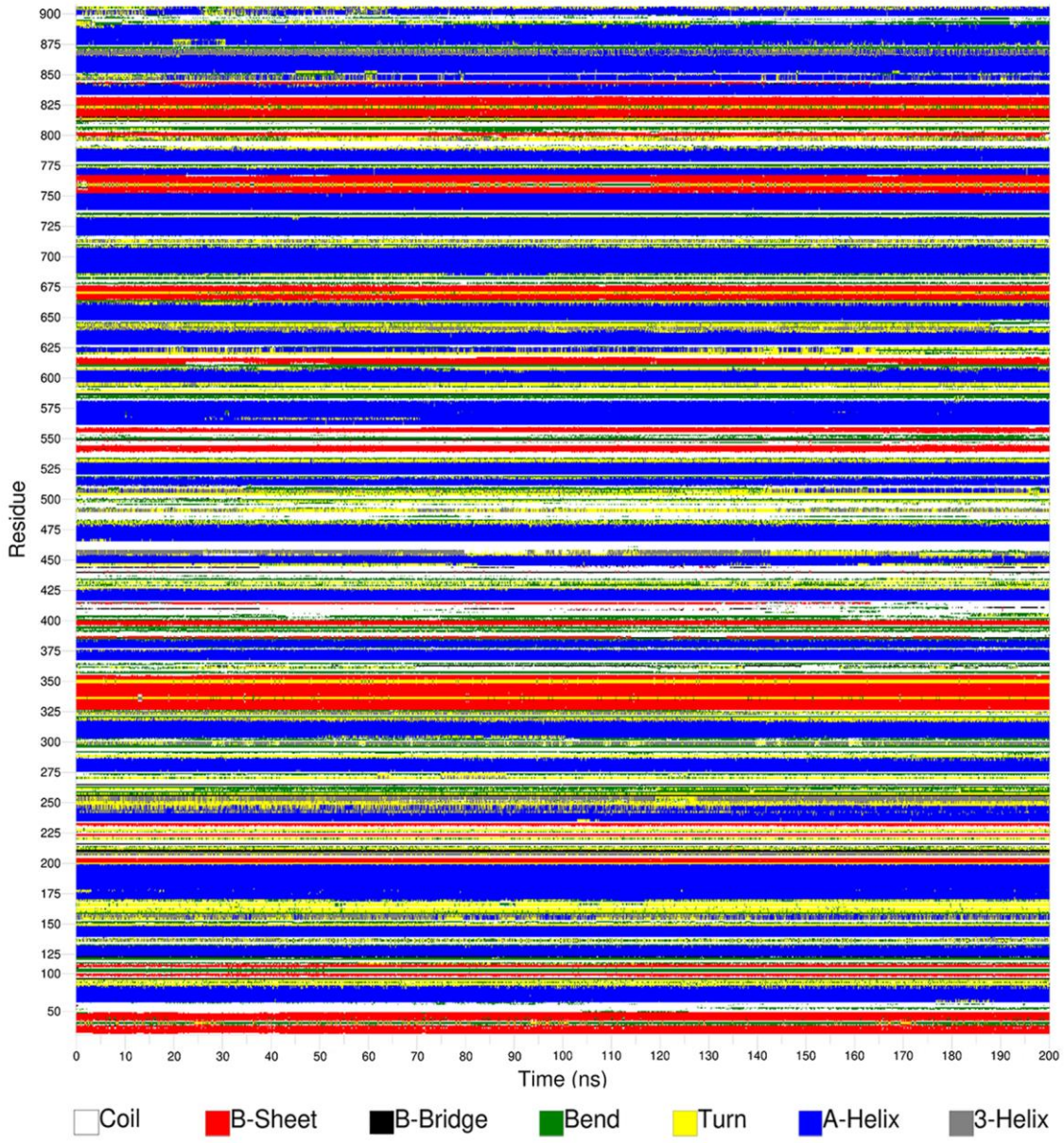

Figure S4. Conformational evolution of secondary structure elements of RdRp in complex with hesperidin during the molecular dynamics simulation period.

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